ACUPUNCTURE FOR THE TREATMENT OF PHANTOM LIMB SYNDROME

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List of publications

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Abstract

Phantom limb syndrome (PLSd) is a prevalent complication post amputation which can be severe and chronic. Multi-disciplinary treatment is recommended, addressing peripheral, central and psychological factors. Although acupuncture is recommended, evidence supporting its effectiveness is sparse. This project aimed to develop an acupuncture protocol for the treatment of lower limb amputees with PLSd and evaluate its acceptability and feasibility prior to a definitive trial.

The project was situated under the Medical Research Council's framework for developing and evaluating complex interventions, and used a multiphase mixed methods research design. Three systematic literature reviews and two studies were undertaken to inform a feasibility study. The literature reviews aimed to identify previous research undertaken on the experience and management of PLSd. The first study, a Delphi study, aimed to develop an acupuncture protocol and the second, a qualitative descriptive study, explored amputees' perceived acceptability of acupuncture within the context of living with PLSd. From these findings a feasibility study was designed and conducted, comprising a randomised controlled trial and semi-structured interviews.

The literature reviews identified limited qualitative studies exploring amputees' experience of PLSd, limited evidence supporting interventions for PLSd and only two non-randomised controlled trials evaluating the effectiveness of acupuncture for treating PLSd. The Delphi study developed a novel acupuncture protocol which was considered 'good practice' and this was used in the feasibility study. The qualitative descriptive study produced rich data, not previously available on a UK demographic group of amputees shortly post amputation, on their experience of PLSd. PLSd was found to be 'real' and bothersome with effects on wellbeing. Additionally, acupuncture was perceived acceptable and outcome measures were identified for use in the feasibility study. The feasibility study generated new original findings on areas which would need addressing before undertaking a definitive trial, including; problems with recruitment, completion of outcomes at one month follow up, blinding, practitioner adherence to the acupuncture protocol, capture of rescue medication and recording of

adverse events. Acupuncture was perceived to be effective at resolving or reducing PLSd.

Findings from this project could inform the development of a definitive trial to establish the effectiveness of acupuncture for treating PLSd.

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Chapter 6. Establishing the feasibility and acceptability of providing acupuncture to lower limb amputees with phantom limb syndrome

Abbreviations

AMPA: Amino-3-hydroxy-5-methylisoxazole-4 proprionic acid

AMSTAR: A Measurement Tool to Assess Systematic Reviews

ARU: Amputee Rehabilitation Unit

BDNF: Brain-derived neurotrophic factor

CAM: Complementary and alternative medicine

CASP: Critical appraisal skills program

CONSORT: Consolidated Standards of Reporting Trials

COREQ: Consolidated criteria for reporting qualitative research

CRPS: Chronic regional pain syndrome

EQ-5D-5L: EuroQol-5 Dimensions

GABA: Gamma-aminobutyric acid

GMI: Graded motor imagery

HADS: Hospital Anxiety and Depression Scale

IMMPACT-II: Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials

IQR: Interquartile range

ISI: Insomnia Severity Index

LOCF: Last observation carried forward

MMR: Mixed methods research

MRC: Medical Research Council

NeuPSIG: Neuropathic Pain Special Interest Group

NHS: National Health Service

NICE: The National Institute for Health and Care Excellence

NMDA: N-methyl-D-aspartate

NPS: Neuropathic pain scale

NPSI: Neuropathic pain symptom inventory

NRES: National Research Ethics Service

NRS: Numerical rating scale

NTPLSd: Not treated phantom limb pain

OSOP: One sheet of paper

PGIC: Patient global impression of change

PICO: Population, intervention, comparator, outcome

PLS: Phantom limb sensations

PLSd: Phantom limb syndrome

PLP: Phantom limb pain

PO: Oral

PQAS: Pain Quality Assessment Scale

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PSS: Perceived Stress Scale

PSS-10: Perceived Stress Scale 10 item

QCA: Qualitative content analysis

R&D: Research and development

RCT: Randomised controlled trial

SF-MPQ: Short Form McGill Pain Questionnaire

SF-MPQ-2: Short Form McGill Pain Questionnaire 2

STRICTA: Standards for reporting interventions in clinical trials of acupuncture

TCM: Traditional Chinese Medicine

TENS: Transcutaneous electrical nerve stimulation

TPLSd: Treated phantom limb pain

TREND: Transparent Reporting of Evaluation with Nonrandomised Designs

VAS: Visual analogue scale

VRS: Verbal rating scale

WMA: Western medical acupuncture

Glossary

List of terms	Definition
Acupuncture	A type of complementary medicine involving the insertion of fine needles into the skin at specific points on the body for the treatment of various physical and mental conditions.
After discharge	The ability of neurons to rhythmically discharge impulses for a relatively long time after cessation of the stimulus.
Allodynia	Pain due to a stimulus that does not usually provoke pain.
Alpha adrenergic receptors	A group of receptors which are the targets of catecholamines especially norepinephrine (noradrenaline) and epinephrine (adrenaline).
Atherosclerosis	The build-up of fatty deposits / plaques in the walls of the arteries restricting blood flow and causing cardiovascular disease.
Catecholamines	Hormones which are released into the blood when a person is under physical or emotional stress. The main catecholamines are dopamine, norepinephrine, and epinephrine.
Central summation	The process by which a sequence of stimuli that are individually inadequate to produce a response are cumulatively able to induce a nerve impulse.
Crossed after discharge	The repetitive synchronous activity in primary afferents inducing firing in neighbours. Crossed after discharge occurs only in spontaneously active neurons and the stimulated neighbour if they share the same dorsal root ganglia. With crossed after discharge single nerve impulses have little effect but repetitive activity in afferent fibres excites non-stimulated neighbours, progressively winding up the discharge rate in passive neighbours.
Cupping	An ancient form of alternative medicine whereby 'cups' are warmed using a flammable substance to remove oxygen to create a vacuum in the cup. The cups are then placed on the skin and the vacuum created by the lack of oxygen means the cups stay anchored to the skin, pulling it upwards. Pumps can also be used instead of a flammable substance to create this suction.
Deafferentation	A loss of the sensory input from a portion of the body.
Deep brain stimulation	An electrical stimulation performed on subcortical areas such as the thalamus or basal ganglia. Motor cortex stimulation involves stimulation of the precentral gyrus.
Deqi	A composite of unique sensations felt by either the acupuncture practitioner, the patient or both, signifying the arrival of 'vital energy'.

Dialectic approach	A research paradigm including different traditional philosophical assumptions regarding reality, knowledge, methodology and values.
Dorsal horn	An anatomical area in the central nervous system / spinal cord. It is composed of neurons which are stimulated by sensory impulses. The apical part of the dorsal horn is called the substantia gelatinosa.
Dorsal root ganglion	A group of nerve cell bodies formed by the cell bodies of the sensory nerves which are located outside the central nervous system and relay information to the central nervous system.
Dysvascular amputation	Amputation due to complication of the vascular system.
Ectopic discharge	Discharge which originates in the axonal endbulb, sprout, patch of demyelination or in the soma (cell body) and not the peripheral sensory ending.
Exteroceptive	Perceptions received from outside of the body, such as touch, temperature and pressure.
Five elements	A philosophy which emphasises the unity of all phenomena in the universe and explains the succession of the seasons. This philosophy is concerned with how humans conform to the laws of nature using the fundamental matter; wood, fire, earth, metal and water.
Gate control theory	The gate control theory was developed by Ronald Melzack and Patrick Wall in 1965. This theory recognised the brain as an active system in pain perception and the dorsal horn as sites of dynamic activity which can modulate afferent input.
Graded motor imagery	A three stage treatment for phantom limb pain which aims to encourage cortical motor networks without triggering pain. It involves limb laterality recognition (a left / right judgement task which requires patients to identify pictures of limbs as being left or right), imagined movements (imagining moving the limb in a smooth and pain free way) and mirror therapy.
Hyperalgesia	Increased sensitivity to a painful stimulus.
Jue yin channel	The paired Liver (LR) and Pericardium (PC) acupuncture channels.
Kinaesthetic	The awareness of the body in space.
Kinetic	Perceptions of movement.
Mirror therapy	A neurorehabilitation technique designed to remodulate the cortical mechanisms of pain.
Motor cortex	The region of the cerebral cortex involved in the planning, control, and execution of voluntary movements.

Moxibustion	A type of Chinese medicine. Moxa is prepared from mugwort leaves (Artemisia vulgaris) and during moxibustion is placed either directly on the skin or held just above it and lit to produce a therapeutic heat over specific acupuncture points or meridians.
Neuroma	Post peripheral nerve injury due to amputation forward growth of the severed nerve is blocked causing the endbulbs and aborted sprouts to form a tangled mass called a neuroma.
Neuromatrix concept	A concept which steered away from the idea of pain as a sensation produced by injury, inflammation or pathology and towards the concept of pain being a multidimensional experience caused by multiple influences.
Nociceptive fibres	Nociceptors allow for alertness of potentially damaging stimuli at the skin by detecting extremes in temperature, pressure and injury-related chemicals. Stimuli are transduced into long-ranging electrical signals that are relayed to higher brain centres.
Pain matrix	The pain matrix was developed from Melazck's neuromatrix concept, but where the neuromatrix concept was not pain specific, the pain matrix was.
Parietal lobe	The area of the brain where information such as taste, temperature and touch are integrated, or processed.
Pattern theory	A pain theory which developed after the specificity theory which stressed central summation mechanisms rather than excessive peripheral stimulation.
Penfield's homunculus	An area of the cortex where body surfaces are mapped.
Phantom limb pain	Painful sensations perceived in the missing portion of an amputated limb.
Phantom limb sensation	Non-painful sensations perceived in the missing portion of an amputated limb.
Phantom limb syndrome	A collective term for phantom limb pain and phantom limb sensations.
Qi	A Chinese term for energy or the body's life force.
Qi gong	An ancient Chinese health care system that integrates physical postures, breathing techniques and focused intention.
Somatosensory cortex	An area of the brain that processes input from the various systems in the body that are sensitive to touch.
Specificity theory	A pain theory which proposed that pain was a specific modality with its own central and peripheral apparatus.
Spinothalamic tract	A central pathway which carries information about noxious stimuli to the brain.
Stump liners	A stocking which can have electromagnetic shielding properties

	to help prevent phantom limb pain.
Sympathetic nervous system	Part of the autonomic nervous system controlling the involuntary part of the nervous system. The sympathetic nervous system tends to predominate in stressful situations and the parasympathetic during rest.
Sympathectomy	A surgical procedure that destroys nerves in the sympathetic nervous system.
Tai chi	A form of Chinese martial arts which is practised to promote health and wellbeing. It involves deep breathing, relaxation and slow controlled movements.
Talipes equinovarus	A deformity of the foot and ankle also known as 'club foot'.
Telescoping	A phenomenon which can occur post amputation where the phantom limb gradually shortens so that the hand or foot becomes closer to the residual limb.
Traditional Chinese Medicine	A systemised style of Chinese Medicine developed in China during the Great Leap Forward and Cultural Revolution (1950-1960s).
Transmission cells	Transmission cells are located in the dorsal horn and project to the brain. Output from these cells depends on afferent input entering the dorsal horn. Transmission cell output is modulated by inhibitory cells in the substantia gelatinosa.
Tui na	A form of Chinese massage / manipulative therapy (including the techniques pushing, kneading, rolling, rubbing and grasping) which is often used in conjunction with acupuncture.
Virtual body	A body image held in the brain such as the somatosensory homunculus. Many different virtual bodies exist.
Western medical acupuncture	An adaptation of Chinese acupuncture, where practitioners do not use the concepts of yin and yang or five elements but instead use knowledge of anatomy, physiology and pathology and the principles of evidence based medicine to guide treatment.
Wind-up	The perceived increase in pain intensity over time when a non-painful stimulus is delivered repeatedly above a critical rate. It is caused by repeated stimulation of group C peripheral nerve fibres, leading to progressively increasing electrical response in the corresponding spinal cord neurons.
Yang ming channel	The paired Stomach (ST) and Large Intestine (LI) acupuncture channels.
Yin-yang	A philosophy in which opposing forces are complementary, interconnected and interdependent and form a dynamic whole.

Chapter 1. Introduction

1.1 Introduction

The aim of the project reported in this thesis was to develop an acupuncture protocol for the treatment of lower limb amputees with phantom limb syndrome and evaluate the feasibility and acceptability of this protocol in preparation for a definitive multi-centred randomised controlled trial. For these reasons, and because acupuncture was considered a complex intervention, this project was structured within the Medical Research Council's (MRC) framework for developing complex interventions (Craig *et al.*, 2008a).

Interest in the effectiveness of acupuncture developed from the author's background as a musculoskeletal physiotherapist and qualified acupuncturist. Through studying acupuncture at MSc level and completing further training in China, the author became interested in the potential for using acupuncture to treat a wide range of conditions and in the evidence underpinning this intervention. An opportunity for further study emerged when Guy's and St Thomas' NHS Foundation Trust opened a new amputee rehabilitation unit within the same building as an established acupuncture department, allowing opportunities for the potential integration of services. Interest in establishing the effectiveness of acupuncture for the treatment of phantom limb pain was expressed, which resulted in the development of this project.

This chapter reviews the prevalence, occurrence and experience of phantom limb pain and phantom limb sensation and discusses management, including acupuncture intervention. The aim and objectives of this project, and structure of the thesis are also outlined.

1.2 Amputation and its associated complication phantom limb syndrome

In the UK, amputation frequently occurs due to diseases such as cancer, peripheral vascular disease, infection, trauma and deformity (NHS, 2014). Diabetes increases the risk of amputation and those with diabetes are estimated to be up to 30 times more likely to undergo amputation than the general population (Diabetes UK, 2014). Of 34,109 lower limb amputations carried out in England over a three year period, 48.9% were in people where diabetes had been coded as a co-morbidity (Holman *et al.*, 2012). A total of 3.2 million people in the UK have been diagnosed with diabetes and by 2025 the number is estimated to have grown to 5 million (Diabetes UK, 2014). With the prevalence of diabetes rising it is likely that so will associated complications (such as peripheral vascular disease and peripheral neuropathy) and medical interventions such as amputation.

Potential complications post amputation are numerous and include; bleeding, congestive heart failure, sepsis, necrosis of the stump, pneumonia, stroke, myocardial infarction, wound infection, urinary tract infections, mortality, stump infarction, chronic stump ulceration and stump deformity (Ploeg *et al.*, 2005, Pollard *et al.*, 2006). Another potential complication is phantom limb pain (PLP) and / or phantom limb sensations (PLS), collectively described in this thesis as phantom limb syndrome (PLSd) unless referring specifically to one or other. PLSd has been recognised as a complication of amputation for many centuries. The American neurologist, Silas Weir Mitchell (1829-1914) coined the term 'phantom limb' (reported in 1866) but the phenomenon was recorded prior to this by Ambroise Paré (1510-1590), René Descartes (1596-1650) and Albrecht von Haller (1708-1777) (Furukawa, 1990, Nathanson, 1988).

PLP is defined as painful sensations perceived in the missing portion of the amputated limb (Davis, 1993). It is neuropathic in nature (Flor, 2002) and caused by a lesion of the somatosensory nervous system (IASP, 2012). PLS are non-painful sensations perceived as emanating from the amputated limb (Melzack, 1992). PLP and PLS are different from each other and should also be distinguished from residual pain (pain perceived as originating in the residual portion of the limb (Davis, 1993)).

1.2.1 Prevalence, occurrence and experience of phantom limb syndrome

Reports on the prevalence of PLP vary considerably, possibly due to differences in measurements, definition, time points of assessment and the study population (Sin *et al.*, 2013) and cut-off points have been found to considerably influence outcomes (from 7-72% when different cut off points for the frequency of PLP were applied (Borsje *et al.*, 2004)). Prevalence of PLP has been reported to be as high as 80% (Ephraim *et al.*, 2005). Two recent surveys of PLP in military personnel each reported a prevalence of 76% (Aldington *et al.*, 2014, Katon and Reiber, 2013) and a nationwide survey in Germany (of which 95.5% were lower limb amputees) reported 75% PLP (Kern *et al.*, 2012). Some studies do report a lower prevalence and a longitudinal study by Bosmans *et al.* (2010) found prevalence of PLP was 32% at six months and 23% at 2 ½ years. However, PLP was classified as present only if amputees suffered PLP a few times a day or more, and absent in cases who reported PLP a few times a week or less. Table 1.1 shows studies reporting on prevalence of PLP and PLS between 2004-2015. These findings suggest that both PLP and PLS are common conditions, which with the rising numbers of diabetes cases and associated complications, may become more frequent in the future.

PLP occurs early post amputation and usually within the first week (Nikolajsen, 2012). Studies report a 67% incidence of PLP 4-5 days post amputation (Hanley *et al.*, 2007) and 72% 8 days post amputation (Jensen *et al.*, 1983). PLP also occurs years later (Foell *et al.*, 2011) and PLP has been reported to occur over two peak periods, the first being within a month of amputation and the second, after a year. Schley *et al.* (2008) found PLP occurred immediately after amputation in 28% of participants, between 1-12 months in 10% and after 12 or more months in 41%. Generally it is assumed that PLP decreases slightly over time with the prevalence rate remaining constant but the duration or frequency of attacks decreasing. However, in one study which reported this trend, 37% were lost to follow up at six months (Bosmans *et al.*, 2010). Other studies suggest PLP does not necessarily improve over time. Schley *et al.* (2008) reported PLP was stable in 38% and worsened in 7% of participants. Hanley *et al.* (2007) found PLP intensity increased by 30% or more in 24% of lower limb amputees over two years, and subsequently reported that time since amputation was not related to pain (Hanley *et al.*, 2009), suggesting that individuals with pain are unlikely to improve over time.

Table 1.1 Prevalence of phantom limb syndrome

Author	Year	Country	Study design	Amputation (UL / LL)	Military study (yes / no)	Number of participants	Time since amputation	PLP (%)	PLS (%)
Aldington *et al.*	2014	UK	CS	UL:17%** LL:83%**	Yes	48	< 13w:n=15 13-26w:n=6 26-52w:n=11 >1y:n=16	49% olm 76% asp	70% olm 66% asp
Katon and Reiber	2013	USA	CS	UL:14% LL:49% Multiple:37 %	Yes	283	M:3.1±1.3y	76%	-
Sin *et al.*	2013	Singapore	CS	LL:100%	No	49	R:4-29m	45%	63%
Kern *et al.*	2012	Germany	CS	UL:4.5% LL:95.5%	No	537	-	75%	73%
Byrne	2011	Cambodia and NZ	CS	LL=86% UL=12% LL+UL=2%	No	58	M:G1;10.4y, G2;15.1y	G1; 52% G2; 69%	G1; 79% G2; 82%
Desmond and Maclachlan	2010	Ireland	CS	UL:100%	No	141	M:50.1y	43%	-
Bosmans *et al.*	2010	Netherlands	L	UL:14% LL:86%	No	85	R:6m-3.5y	6m=35% 3.5y=33%	-
Probstner *et al.****	2010	Brazil	CS	LL:92% UL:8%	No	75	M:49m R:0-247m	47%	91%
Davidson *et al.*	2010	Australia	CS	LL:67% UL±LL:33%	No	57	0-1y:29% 2-5y:65% >5y:5%	90% of those reporting pain*	-
Modirian *et al.*	2009	Iran	CS	Bilat UL:100%	Yes	103	M:205.9m R:28-311m	54%	82%
Ebrahimzadeh and Hariri	2009	Iran	CS	LL:100%	Yes	200	M:17.4y R;15-22y	17%	54%
Hanley *et al.*	2009	America	CS	UL:100%	No	104	Md:7y R:0.2-60.3y	79%	81%
Schley *et al.*	2008	Germany	CS	UL:100%	No	96	Md:3.2y R:0.9-3.8y	45%	54%
Ketz	2008	USA	CS	UL:23% LL:90%	Yes	30	<5y	77%	-
Hanley et al.	2007	USA	L	LL:100%	No	57	4-5d-24m	4-5d:67% 6m:69% 12m:73% 24m:62%	-
Richardson *et al.*	2006	UK	L	LL:100%	No	52	6m	79%	100%
Desmond and Maclachlan	2006	Ireland	CS	UL:16.5% LL:81.6% UL+LL:1.9%	No	582	M:53.3y R:10-65y	70%	-
Hanley *et al.*	2006	USA	CS	LL:100%	No	255	M:14.2y Md:7y R:6m-74y	72%	-
Ephraim *et al.*	2005	USA	CS	UL:10.9% LL:88.9%	No	552	Md:4y R:1-66y	80%olm	-

Key: UL, upper limb; LL, lower limb; d, days; w, weeks; m, months; y, years; R, range; M, mean; Md, median; G1, group 1; G2, group 2; olm, over the last month; asp, at some point; L, longitudinal; CS, cross-sectional; *84% of UL and 64% of LL amputees reported pain; **the study included double amputees (n=23%), triple amputees (n=6%) ***study included cancer participants only.

Note: studies were identified through the database Pubmed using the search terms: (phantom limb [MeSH]) AND ("epidemiology" OR "prevalence" OR "survey").

This is supported by studies reporting on the chronicity of PLP. Studies report PLP may be present for many years. A prevalence of 43% mean time 50.1 years post amputation has been reported (Desmond and Maclachlan, 2010) as has a prevalence of 52% and 69% mean time 10.4 and 15.1 years post amputation in a smaller study with two different cohorts (Byrne, 2011).

No association between PLP and age, gender, level and aetiology of amputation, marital status and amount of post-surgical pain medication has been found (Hanley *et al.*, 2007, Hanley *et al.*, 2009). No significant difference has been identified in prevalence and intensity of PLP between diabetic and non-diabetic amputees (Clark *et al.*, 2013). Cultural, social and economic environment do not appear to influence development of PLP (Byrne, 2011). The intensity of PLP experienced is similar in lower limb amputees regardless of level of amputation (Behr *et al.*, 2009). One longitudinal study found that the chance of suffering PLP was lower for men and lower limb amputees compared to women and upper limb amputees (Bosmans *et al.*, 2010). Other literature reports that pain is more likely, more severe and longer lasting in upper limb amputees than lower limb amputees (Davidson *et al.*, 2010). Individuals experiencing PLP may tend to be older than those not experiencing it and males and females may vary in their experience of PLP (Gallagher *et al.*, 2001). A study on amputees investigating sex differences in pain intensity, pain interference and pain related coping found no significant sex difference in the presence or intensity of amputation related pain. However, females did report overall greater pain intensity and pain interference and endorsed significantly greater pain catastrophising and use of several adaptive and maladaptive pain coping strategies (Hirsh *et al.*, 2010). Retrospective studies have shown that low educational status and untreated depressive symptoms are more common in amputees with PLP than those with no pain (Byrne, 2011).

Literature suggests that PLP is usually intermittent and varying frequencies have been reported, from 20 days out of a month to less than once per month (Gallagher *et al.*, 2001). Davidson *et al.* (2010) found 33% of lower limb amputees and 94% of upper limb ± lower limb amputees reported experiencing pain most days to every day. Desmond and Maclachlan (2010) reported duration of pain attacks and found in 43% attacks lasted seconds or a few minutes, in 20% several minutes to hours and longer for the rest.

Although PLP is usually intermittent, constant pain and sensations have been reported. Desmond and Maclachlan (2010) reported constant pain or pain most days in more than one third of amputees 50.1 years mean time since amputation. Kern *et al.* (2012) reported constant pain in 28% of participants (but average time post amputation was not provided).

PLP can be of moderate / severe intensity. Davidson *et al.* (2010) found 28% of lower limb amputees reported moderate to severe pain measured on an eleven point numerical pain rating scale where 0-3 was classified as no / mild pain and 4-10 as moderate / severe pain. This correlates with an earlier study by Ehde *et al.* (2000) who reported 30% of amputees suffered severe intensity PLP (mean intensity 5.1 measured on an eleven point scale). More recently a large study by Kern *et al.* (2012) reported pain intensity ranging between 5.2 and 7.5 measured on an eleven point scale suggesting that intensity of PLP has not improved over recent years.

Sensations frequently experienced with PLP include; shooting, pricking, burning, stabbing, pins and needles, tingling, throbbing, cramping and crushing (Nikolajsen, 2012). The strongest sensations of PLP tend to come from body parts with the highest brain cortical representation, such as fingers and toes (Manchikanti and Singh, 2004) and PLP is primarily localised to the distal parts of the missing limb (Nikolajsen, 2012). Amputees with worse nocturnal pain are more likely to report spontaneous limb movements such as jerking, jolting and spasms (Giummarra and Bradshaw, 2010).

PLP may be modulated by internal and external factors. Exacerbation of PLP may be produced by physical or emotional stimuli. Anxiety, depression, urination, cough, defecation, sexual activity, cold environment or changes in the weather may worsen symptoms (Manchikanti and Singh, 2004) as may walking / prosthesis use and stress (Davidson *et al.*, 2010). Time of day may also affect PLP with pain worsening as the day progresses, being worst at night. Pain at night may be associated with an urge to move the phantom and residual limb to relieve discomfort (Giummarra and Bradshaw, 2010). PLP can impact subjective well-being (Bosmans *et al.*, 2007) and physical and mental components of quality of life, hindering mobility and impacting on psychological state (Sinha *et al.*, 2011). In a survey by Ephraim *et al.* (2005) 28.7% of amputees surveyed were found to have symptomatology of depression and amputees with pain were more

likely to have symptoms of depression than those without pain. Gallagher *et al.* (2001) found PLP had repercussions on physical rehabilitation, interfering with prosthetic training causing a reduction in walking ability.

Factors which cause extreme arousal have been reported to ease PLP, including extremely hot or cold baths, eating, social stimulation such as arguing and physical stimulation such as hard rubbing (Giummarra and Bradshaw, 2010). Other coping methods include distraction, physical exercise, stump manipulation and alcohol consumption (Ketz, 2008) and relaxation, seeking support, and drugs (Whyte and Niven, 2001).

Phantom limb sensations

PLP, PLS and stump pain are an inter-related phenomenon (Ketz, 2008, Richardson *et al.*, 2006). Kooijman *et al.* (2000) found a significant association between PLP and PLS with PLP being present in 36 of 37 amputees with PLS, but only 1 of 17 with no PLS. Hanley *et al.* (2009) found 86% of amputees who reported having PLS also suffered PLP.

PLS tends to be more prevalent than PLP with Richardson *et al.* (2006) reporting a prevalence of 100%. PLS usually starts within a couple of days of amputation (Schley *et al.*, 2008) and like PLP is a chronic condition which may be present for many years. PLS can be divided into exteroceptive (perceptions of, for example, touch, pressure, tingling, temperature), kinetic (perceptions of movement) and kinaesthetic (perception of size, shape or position of the limb) perceptions (Hsu and Cohen, 2013). Exteroceptive sensations are frequently reported as tingling, tightness and pins and needles (Hill, 1999). Immediately post amputation the phantom limb usually resembles the pre-amputation limb in shape, volume and length (Hill, 1999) but over time the limb may undergo 'telescoping' in which the phantom limb gradually appears to shorten, with the hand or foot shifting closer to the residual limb (Nikolajsen and Jensen, 2001). This phenomenon occurs in approximately ¼ to $^{2}/_{3}$ of major limb amputations (Hsu and Cohen, 2013). During telescoping, the last body parts to disappear are those with the highest representation in the cortex (Hill, 1999).

1.2.2 Treating phantom limb syndrome

Treatment of PLSd should take a multidisciplinary approach, addressing peripheral, central and psychological factors (Le Feuvre and Aldington, 2014). Options available include; invasive interventions, pharmacology and supportive non-pharmacological non-invasive interventions (Knotkova *et al.*, 2012).

Invasive interventions such as surgical removal of neuroma, thermal nerve root destruction, spinal ganglionectomy and dorsal root entry zone lesions, lead to unrestorable nervous tissue damage, high rates of complications and high rates of recurrent pain. They are generally considered unsuccessful and not usually used (Knotkova *et al.*, 2012).

Currently no pharmacological guidelines exist for the treatment of PLSd (Fang *et al.*, 2013). Guidelines for the treatment of neuropathic pain include offering a choice of amitriptyline, duloxetine, gabapentin or pregabalin. Tramadol should only be considered for acute rescue therapy (NICE, 2013). The European Federation of Neurological Societies recommends pregabalin, amitriptyline or gabapentin as first line treatment and tramadol as second line. Strong opioids have been recommended as second or third line intervention if long term treatment is not an issue (Attal *et al.*, 2010) but should not be considered as first line medication due to issues with dependence and tolerance (Finnerup *et al.*, 2007). In the UK the most common first line medication is gabapentin and most treatments only include one therapeutic class. Analgesics alone (opioid +/-non opioid) are prescribed in 38% of cases (Hall *et al.*, 2013) suggesting that PLSd is treated in line with neuropathic pain guidelines. However, as discussed in the literature review (section 2.6.2.3) little evidence is available supporting the use of gabapentin for PLSd.

Frequently recommended supportive non-pharmacological non-invasive treatments include stump liners, graded motor imagery (GMI) and mirror therapy alone. Acupuncture has also been recommended (Le Feuvre and Aldington, 2014). Stump liners work on the hypothesis that changes in electro-magnetic fields aggravate PLSd due to changes in serotonin metabolism, which plays a role in pain through descending inhibition (Giummarra *et al.*, 2011). GMI is a three stage treatment which aims to

encourage cortical motor networks without triggering pain (Bowering *et al.*, 2013). It involves limb laterality recognition (a left / right judgement task which requires patients to identify pictures of limbs as being left or right), imagined movements (imagining moving the limb in a smooth and pain free way) and mirror therapy (Bowering *et al.*, 2013). Mirror therapy was first introduced as a standalone treatment by Ramachandran in the 1990s (Ramachandran and Altschuler, 2009) and is a neurorehabilitation technique designed to remodulate the cortical mechanisms of pain. The mirror creates a visual illusion so that movement of the unaffected limb is superimposed on the residual limb providing positive feedback to the motor cortex of movement of the affected limb. This is supposed to interrupt the pain cycle and therefore reduce or eliminate pain (Kiabi *et al.*, 2013). Somatosensory reorganisation is partially reversed with mirror therapy suggesting that PLSd is reduced through mirror therapy influencing cortical reorganisation (Foell *et al.*, 2014). As integration of an external object into a person's body representation is influenced by the degree of congruency (deviation between the felt and seen position of the limb impedes the sensation of ownership) mirror therapy may not be effective in amputees with perceived distortions of their phantom (Foell *et al.*, 2014).

Despite Le Feuvre and Aldington (2014) recommending a multidisciplinary approach for the treatment of PLSd, as with pharmacological approaches there is little evidence available supporting the use of these non-pharmacological interventions. This is discussed in the literature review (section 2.6) justifying the need for further research to develop robust interventions for the management of PLSd.

1.3 Defining acupuncture

Acupuncture and moxibustion are one of the earliest healing methods in the history of Chinese medicine, pre-dating herbal medicine (Ma, 2000). The use of stone needles 'Bian Shi' was reported in the *Shanhai Jing* (Classics of Mountains and Seas), written during the Warring States (475-221 BC) and bone needles dating from as early as the Xia and Shang Dynasties (21st-11th Centuries BC) have been identified (Ma, 2000).

Acupuncture in China as it is known today emerged over many centuries. During the 21st Century BC to 476 BC the philosophical thinking of yin-yang and the five elements appeared. During the Warring States Period (475-221 BC) metal needles were developed (the book the *Miraculous Pivot* records nine types of metallic needles) and *bian* stone needles were replaced (Xinnong, 1999). Between the 5th and 1st Century BC, the *Huangdi Neijing* (Yellow Emperor's Internal Classic) was written by a number of scholars and physicians, containing two parts, the *Su Wen* Plain Questions and the *Ling Shu* or Miraculous Pivot. This book adopted a yin-yang and five element philosophy and reported extensively on acupuncture (Ma, 2000). In 256-260 AD the medical doctor Huangfu Mi compiled a systemised book on acupuncture and moxibustion, the Systematic Classic of Acupuncture and Moxibustion (Xinnong, 1999) and from the 3rd Century AD, acupuncture became a specialised discipline which was often handed down through the generations. It was officially recognised by the Imperial Medical Bureau of the Tang Government in 618 AD (Ma, 2000) and during the Song government (approx. 987-1067 AD) the Illustrated Classic of Acupuncture and Moxibustion as Demonstrated on Bronze Figure was compiled and two bronze life-size acupuncture figures manufactured (Ma, 2000).

However, in the 17th Century, herbal medicine was deemed superior to acupuncture and acupuncture lost popularity. During the Opium War in 1840, with the introduction of Western Medicine, acupuncture further lost favour and in 1914 was banned by the government of China. With the founding of the People's Republic of China, during the Great Leap Forward in the 1950s and the Cultural Revolution in the 1960s, acupuncture was promoted by Chairman Mao Zedong as a pragmatic solution to providing an under resourced China with health care (Ramey and Buell, 2004). During this time the theory of acupuncture and moxibustion was systematised (Xinnong, 1999). This style of

acupuncture is currently taught in China and the UK as traditional Chinese medicine (TCM) acupuncture. TCM encompasses a diversity of interventions; acupuncture, moxibustion, cupping, Chinese Herbal Medicine, tui na, dietary therapy, tai chi and qi gong. Colleges and universities teaching TCM acupuncture in the UK usually include education on moxibustion, cupping, dietary therapy, tui na and tai chi / qi gong and treatment by a TCM trained acupuncture practitioner may include any of these associated treatments (British Acupuncture Council, 2011).

Other styles of acupuncture which have emerged include five element acupuncture and western medical acupuncture (WMA). Five element acupuncture was founded by Professor Worsley (1923-2003) in the 1960s and 1970s. Worsley drew on passages in the Nei Jing and Nan Jing and also studied in Taiwan, Singapore and Korea. Five element acupuncture is based on the principle that every human being has one true cause of disease (or causative factor) and when this is correctly diagnosed through pattern identification, the treated presenting signs and symptoms disappear (Hicks *et al.*, 2004). WMA is an adaptation of Chinese acupuncture, where practitioners do not use the concepts of yin, yang and qi (vital energy). Instead WMA uses the knowledge of anatomy, physiology and pathology and the principles of evidence based medicine to guide treatment. Treatment principles may include minimal needling, identification of treatment areas on the body suitable for acupuncture, subcutaneous needling over active trigger points or attempts to match therapy with neurophysiological concepts. It is practiced predominantly by conventionally trained practitioners including conventional doctors, nurses, physiotherapists and other healthcare practitioners working within the western health service (White, 2009).

1.3.1 Acupuncture use and provision in the UK

Acupuncture in its varying styles is widely available both in the NHS and private practice. It is practiced by a range of health care practitioners including general practitioners, allied health professionals, and acupuncturists. The Acupuncture Association of Chartered Physiotherapists has over 6000 members, the British Acupuncture Council around 3000 and the British Medical Acupuncture Society around 2300 members. Independent acupuncturists predominately practice TCM style acupuncture (90%) and over one third of physiotherapists trained in acupuncture also use this style (Hopton *et*

al., 2012).

It has been estimated that approximately 3.8 million acupuncture treatments are provided annually, predominately in independent clinics outside of the NHS (Hopton *et al.*, 2012). Data from an English nationwide survey found that lifetime prevalence of using complementary and alternative medicine (CAM) was 44%, with massage, aromatherapy and acupuncture most commonly used (Hunt *et al.*, 2010). Individuals most frequently seek acupuncture intervention for musculoskeletal complaints (low back pain, cervical pain, shoulder pain and knee pain) and headaches and migraines (Hopton *et al.*, 2012) suggesting individuals in the UK predominately use acupuncture for pain relief.

Many systematic reviews have been undertaken evaluating the effectiveness of acupuncture for treating different pain states and tend to report favourably (Cho *et al.*, 2015, Manyanga *et al.*, 2014). A robust systematic review, evaluating the effectiveness of acupuncture for chronic pain which included only randomised controlled trials (RCTs) where allocation concealment was deemed adequate (31 included trials) found acupuncture to be superior to both no acupuncture and sham acupuncture for the treatment of chronic pain. Although findings were modest, data indicated that acupuncture was more than a placebo (Vickers *et al.*, 2012). However, the effectiveness of acupuncture specifically for treating PLSd has not been widely assessed or documented, with most of the literature consisting of case reports. A systematic review by Mannix *et al.* (2013) including English papers only, evaluating the effectiveness of acupuncture for treating PLSd, identified 16 studies, of which ten were case studies, three cross-sectional studies, two case-study series and one a non-randomised controlled trial.

Acupuncture is a relatively safe intervention (MacPherson *et al.*, 2004, Wheway *et al.*, 2012, Witt *et al.*, 2009). A systematic review on the incidence of adverse events found needle pain, tiredness and bleeding were most commonly reported. The incidence of serious adverse events (pneumothorax and needle fracture resulting in surgical removal of the fragment) was 0.001% for both, with pneumothorax occurring only twice in nearly 250,000 treatments (Ernst and White, 2001). A systematic review of Chinese literature identified 115 articles, including 479 cases of adverse events. Increased frequencies of

serious adverse events, including those not commonly reported in UK, were reported (spinal epidural haematoma, subarachnoid haemorrhage, pneumothorax, injury of abdominal organs and eyes). However, reports of these serious adverse events may be due to acupuncturists in rural China rarely receiving formal education (Zhang *et al.*, 2010). There is no evidence supporting the transmission of infection through acupuncture in the UK. Transmission of hepatitis B has been related only to inadequate sterilisation of reusable needles and acupuncturists who were hepatitis B IgM positive. There have been no cases of HIV, hepatitis C or Variant Creutzfeldt-Jacob Disease related to acupuncture (Walsh, 2001).

Acupuncture is widely available, safe and well utilised in the UK for the treatment of pain and the above systematic reviews suggest acupuncture may be effective in treating a range of painful conditions. Amputees may benefit from access to this intervention as part of their multidisciplinary care package within the NHS. However, conclusions cannot be drawn from the current literature and a high quality RCT is needed to provide evidence of acupuncture's effectiveness / ineffectiveness for treating PLSd.

1.4 Framework of the project and research aim and objectives

As described later, in chapter 3, this thesis is made up of three separate studies. To aid clarity, when discussing the studies as a whole, the term 'project' has been used and when discussing each individual study, the term 'study' has been used. Due to the nature and complexity of the intervention researched in this project, the project was situated under the MRC framework for developing and evaluating complex interventions (Craig *et al.*, 2008a) and this framework was used to guide the research (section 3.2). The developmental stages of the MRC framework requires reviewing literature, and therefore this project's objectives included this stage. Because the project's objectives were developed in keeping with the MRC framework (table 3.1) and therefore included objectives on literature reviews, the aim and objectives in this thesis are given in the introduction (figure 1.1 and the component points in relation to the three sequential studies in figure 1.2). Justification for undertaking the developmental studies included in this project are reported after the literature review (section 2.8).

As described in chapter 3, methodologically the project was considered mixed methods research (MMR) consisting of three independent studies, all developed to answer the aim of the project. The thesis presents these as three separate but related studies. To address the project aim and objectives, the three studies were undertaken sequentially with the results of one influencing the design of the next. Consequently they are presented sequentially in the thesis but the underlying methodology and overall concept is described in chapter 3.

Chapter 2, literature review, provides a narrative overview of pain theories and the mechanisms of PLSd. Three reviews, completed systematically, are reported to identify amputees' experience of PLSd, evidence supporting the management of PLSd, and evidence on the effectiveness of acupuncture for treating this pathology. For completeness, to access Chinese and Korean databases, evidence on the effectiveness of acupuncture for treating PLSd was undertaken in collaboration with Korean and Chinese colleagues. Therefore, only a brief summary of these findings is reported in this thesis and the published articles included in the appendix (appendix 2.4 and 2.5). Chapter 3, methodology, describes the overarching methodological and conceptual framework of the project, the paradigm under which the project was situated and the

methodology employed. The first study, presented in Chapter 4, developing an acupuncture protocol for treating lower limb amputees with PLSd, was a Delphi consensus study, undertaken to develop an acupuncture protocol for treating PLSd. The second study, presented in Chapter 5, exploring the acceptability of acupuncture intervention within the context of living with PLSd and identifying outcome measures for use in a feasibility study, was a qualitative descriptive study, involving interviews with lower limb amputees to gain insight into the acceptability of acupuncture and to identify appropriate outcome measures for use in the third study. The third study, presented in Chapter 6, establishing the feasibility and acceptability of providing acupuncture to lower limb amputees with PLSd, was a feasibility study which was undertaken to inform on the feasibility of acupuncture for treating PLSd before designing a definitive trial. Chapter 7, conclusion, reflects on the project, highlights new knowledge, considers its implication for clinical practice and future research, acknowledges its limitations and provides an overall summary of findings.

1.4.1 Defining acupuncture in this thesis

In keeping with MRC guidelines on what constitutes a complex intervention (discussed in section 3.2) acupuncture was considered to be a complex intervention and was considered from a predominately TCM viewpoint. This was partly because TCM is used by approximately 90% of independent acupuncturists and by over one third of physiotherapists (Hopton *et al.*, 2012) and partly because of the author's background and training. However, when applicable, other styles of acupuncture were recognised and discussed. The term 'acupuncture' was considered to solely mean the insertion of acupuncture needles, but information on the use of adjunctive treatments was captured when relevant. Adjunctive treatments were included in the feasibility study (Chapter 6) partly because the author wanted to stay as close as possible to the roots of TCM acupuncture clinical practice and allow intervention to be similar to a typical TCM acupuncture treatment, and partly because complex interventions should evaluate practical effectiveness (whether the intervention works in clinical practice (Craig *et al.*, 2008a)).

Figure 1.1 Project aim and objectives

Aim:

To develop an acupuncture protocol for the treatment of lower limb amputees with PLSd and evaluate its acceptability and feasibility prior to undertaking a definitive multi-centred randomised controlled trial.

Objectives:

Literature review:

1. Review literature on amputees experience of PLSd.
2. Identify relevant research evaluating the effectiveness of interventions to prevent or manage PLSd.

Delphi study:

3. Develop an acupuncture protocol for the management of PLSd in lower limb amputees for use in a feasibility study.

Qualitative descriptive study:

4. Explore lower limb amputees perceived acceptability of acupuncture within the context of living with PLSd, appropriateness of outcome measures and willingness to be involved in a randomised controlled trial.

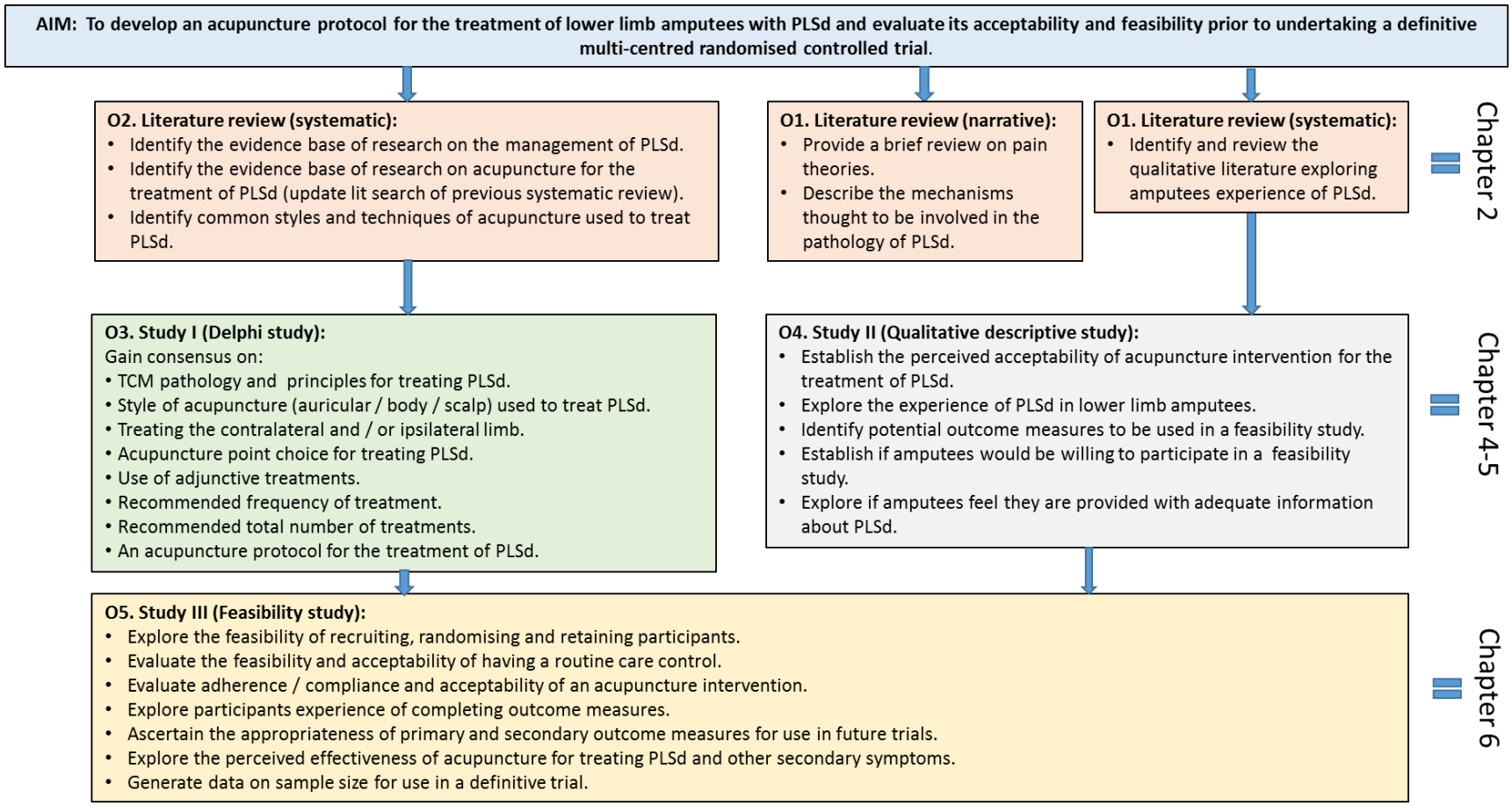
Feasibility study:

5. Evaluate the feasibility and acceptability of providing acupuncture intervention to a group of lower limb amputees in preparation for a definitive multi-centred RCT evaluating the effectiveness of acupuncture for treating PLSd.

Chapter 2 = Chapter 4 = Chapter 5 = Chapter 6

Key: PLSd, phantom limb syndrome.

Figure 1.2 Project aim and objectives in relation to each stage of the project and each individual study



Key: O, objective; PLSd, phantom limb syndrome; TCM, traditional Chinese medicine; lit, literature.

1.5 Summary

PLSd is a frequent complication post amputation and is a prevalent condition. With the numbers of amputations on the rise, so too may be the prevalence of PLSd.

Different treatment approaches exist for the management of PLSd and a multidisciplinary approach is advised. Acupuncture is an accessible intervention both within NHS physiotherapy departments, and in private health care. Evidence suggests it may be effective at treating a variety of painful conditions but as reported later, in chapter 2, little evidence supports its specific use for treating PLSd.

The aim of this project was to develop an acupuncture protocol for the treatment of lower limb amputees with PLSd, which could be implemented in a multi-centred RCT to determine effectiveness. To achieve this aim the project situated itself under the MRC framework for developing complex interventions, used MMR methodology and consisted of three separate sequential studies.

The next chapter includes a critical review of the literature on the experience and treatment of PLSd.

Summary of introduction

- PLSd is a prevalent condition.
- Many different treatment approaches exist for the management of PLSd and a multidisciplinary approach is recommended.
- Evidence suggests acupuncture may be effective and safe for treating a variety of different pain states.

Chapter 2. Literature review

2.1 Introduction

This chapter reviews literature on the mechanisms, experience and treatment of PLSd. Before the literature review the objectives specific to this chapter are identified. The chapter begins with a narrative review (a type of literature review which aims to summarise previous work and does not necessarily include a comprehensive search strategy or quality appraisal (Grant and Booth, 2009)). This review aimed to report briefly on pain theories and the mechanisms currently thought to be involved in the pathology of PLSd. This was not reviewed systematically, partly because a narrative review was considered the most suitable approach for this type of literature and partly because it was not considered to directly affect the design of this research project. It was included to give context to PLSd and to provide background information.

Three reviews, undertaken systematically are then documented. These reviews aimed to answer some of the questions posed within the developmental stage of the MRC framework for developing and evaluating complex interventions (table 3.1). The reviews aimed to identify previous research undertaken on the experience and management of PLSd, to identify steps which would need to be undertaken to fulfil this project's aim. The first, a qualitative review and meta-synthesis, explored amputees' experience of PLSd. This was undertaken to inform the author of amputees' experiences of PLSd and to confirm whether a feasibility study was necessary, through understanding whether PLSd was considered problematic to amputees. The second, a review of systematic reviews, was undertaken to identify if there was evidence supporting the use of current interventions for managing PLSd. This was completed to establish if other treatment approaches were needed. The third, an updated literature search of a quantitative review originally undertaken with Chinese and Korean colleagues, was undertaken to establish whether further research were needed to evaluate the effectiveness of acupuncture for treating PLSd. It was also undertaken to identify common trends in treatment approach, to help develop an acupuncture protocol for use in a feasibility study. Through completing these literature reviews, justification for the three studies included in this project is provided.

2.2 Objectives

This chapter addressed the project objectives described in the introduction (figure1.1):

- Review literature on amputees' experience of PLSd.
- Identify relevant research evaluating the effectiveness of interventions to prevent or manage PLSd.

As described in the introduction (figure 1.2) the component parts of these objectives were to:

- Provide a brief review on pain theories.
- Describe the mechanisms thought to be involved in the pathology of PLSd.
- Identify and review the qualitative literature exploring amputees' experience of PLSd.
- Identify the evidence base of research on the management of PLSd.
- Identify the evidence base of research on acupuncture for the treatment of PLSd (update literature search of previous systematic review).
- Identify common styles and techniques of acupuncture used to treat PLSd.

2.3 A brief review of pain theories

Pain is a multi-system output, associated with actual or potential damage. It is produced when the brain perceives the body is in danger and action is required (Moseley, 2003a). Pain is usually associated with injury, however, it is possible to have injury without pain and pain without injury. Pain intensity does not correspond with the amount of tissue damage (Moseley, 2003a) and can persist long after tissues have healed (Melzack and Wall, 2008).

Prior to 1965, there were two main opposing theories of pain, the specificity theory and the pattern theory. However, in 1965 Melzack and Wall proposed an alternative theory, the gate control theory of pain (Moayedi and Davis, 2013). Melzack subsequently developed the neuromatrix concept in 1989 (Iannetti and Mouraux, 2010). This concept steered away from the idea of pain as a sensation produced by injury, inflammation or pathology and towards the concept of pain being a multidimensional experience caused by multiple influences (Melzack, 1999). From the neuromatrix concept the pain matrix was developed but where the neuromatrix was not restricted to the perception of pain, the pain matrix was partially pain specific (Iannetti and Mouraux, 2010). These theories are described briefly below.

The specificity theory proposed that pain was a specific modality with its own central and peripheral apparatus. It was understood that there were dedicated pathways for each somatosensory modality which projected to a specific pain centre in the brain. Pain receptors (i.e. free nerve endings) generated impulses which travelled along nociceptive fibres in the peripheral nerves and in the spinothalamic tract centrally to a pain centre in the thalamus (Melzack and Wall, 1965).

As a reaction against the specificity theory, other theories were proposed which were grouped under the general term of pattern theory (Melzack and Wall, 1965). Theories were proposed which stressed central summation mechanisms rather than excessive peripheral stimulation (Moayedi and Davis, 2013). Related to central summation was the theory that a specialised input-controlling system normally prevented summation from occurring and that it was destruction of this system that led to pathological pain states (Melzack and Wall, 1965). Although the concepts of central summation and input

control had the ability to explain many aspects of pain which specificity theory could not, there was no explicit role for the brain other than passively as a receptor of messages (Melzack, 1993).

An alternative model, the gate control theory recognised that the perception of pain was more complex than simple receiving and recording. The role of the brain as an active system and the dorsal horn as sites of dynamic activity (inhibition, excitation and modulation) were included in the theory (Melzack, 1993). The gate control theory stated that the substantia gelatinosa in the dorsal horn functioned as a gate, modulating afferent input before it influenced transmission cells. Afferent patterns in the dorsal column acted as a central control trigger, activating brain processes that influenced gate modulation. Transmission cells activated neural mechanisms which were responsible for the perception of pain (the action system). The action system was activated when the output of transmission cells exceeded a critical level. Large (Aβ) fibres had a negative feedback mechanism, supressing the transmission of small nociceptive fibres whereas small fibre activity had a positive feedback mechanism, exaggerating the effects of arriving impulses. The central effects of peripheral stimulus were determined by the total number of active fibres, frequencies of nerve impulses and proportion of large and small fibres activated (Melzack and Wall, 1965). A summary of the gate control theory is described in figure 2.1.

After the gate theory, the neuromatrix was designed as a template of the whole, providing a neural pattern / neural signature for the body. The neuromatrix provided feelings of complex qualities from the body, visual images and knowledge of the self and meanings of body parts in terms of social norms (Melzack, 1993). The neuromatrix concept recognised that the area of brain involved in the experience and behaviour of pain was extensive (Melzack, 2001). Imaging studies support this showing no single pain centre, with many cortical areas being activated during pain (Moseley, 2003a). With the neuromatrix concept, it is thought that pain develops when homeostasis fails and the neuromatrix produces destructive conditions which give way to pain (Melzack, 2001). A summary of the neuromatrix concept is described in figure 2.2.

Figure 2.1 The Gate Control Theory

- Nerve impulses from afferent fibres are modulated in the substantial gelatinosa area of the dorsal horn before they influence transmission cells. (The substantia gelatinosa functions as a gate).
- Activity in large and small diameter afferent fibers influence the spinal gate. Large fiber activity closes the gate and small fiber activity opens it.
- Descending nerve impulses from the brain influence the spinal gate.
- The central control trigger is a specialised system of large-diameter rapidly conducting fibres. It activates selective cognitive processes. Descending fibers then modulate the spinal gate.
- The action system is neural areas that underlie complex sequential patterns of behavior and experience characteristic of pain. The action system is activated when the output of spinal cord transmission cells exceeds a critical level.

(Melzack, 1993)

Figure 2.2 The Neuromatrix Concept

- The body one normally feels is subserved by the same neural processes in the brain. These processes are normally activated and modulated by input from the body but can also act in the absence of any input.
- All qualities, including pain, which are normally felt by the body are also felt in the absence of input from the body.
- The body is identified as the 'self' and is perceived as a unity which is distinct from other people and the surrounding world. The experience of the self as a point of orientation in the environment is produced by central neural processes and is not derived from the peripheral nervous system or spinal cord.
- The brain processes that underlie the body-self are built in by genetic specification and are modified by experience.

(Melzack, 1999)

The pain matrix was derived from the neuromatrix and referred to cortical areas which are frequently involved in pain. Unlike the neuromatrix concept, the pain matrix implied that the pattern of responses in the brain to nociceptive stimuli is specific (Iannetti and Mouraux, 2010). The discriminative (pain intensity) aspect of pain was viewed to be represented in the primary (S1) and secondary (S2) somatosensory cortices and the affective (unpleasantness) aspect of pain was viewed to be represented in the anterior cingulate cortex, insula, ventral prefrontal lobe, amygdala and adjacent hippocampus (Lotze and Moseley, 2007).

A critical component of the pain matrix is the concept of body image (Lotze and Moseley,

2007) and that pain is experienced by the 'virtual body', a body image held in the brain (Moseley, 2003a). The most well-known spatial representation of the internal and external physical environment is the primary somatosensory homunculus but there are others, and different virtual bodies may dominate experience at different times (Moseley, 2003a). The virtual body is an important aspect of the pain matrix because it provides a neural substrate for pain to be allocated an anatomical reference. The virtual body is continually updated by sensory input and can be modulated by psychosocial factors, memory and beliefs (Lotze and Moseley, 2007). It undergoes profound changes in response to persistent pain, making it more sensitive to noxious and non-noxious input (Moseley, 2003a). It also undergoes change in response to cognitive-evaluative input (Moseley, 2003a).

Summary of pain theories

- The main theories of pain include the specificity, pattern, gate control, neuromatrix and pain matrix theories.
- The specificity theory proposed specific pain receptors in the body project to a pain centre in the brain.
- The pattern theory introduced the idea of central summation.
- The gate control theory recognised the brain as an active system and the dorsal horn as a site of dynamic activity.
- The neuromatrix concept acts as a template for the whole.
- The pain matrix was developed from the neuromatrix concept and includes the concept of body image and virtual bodies.

2.4 Mechanisms involved in the pathology of phantom limb syndrome

Amputation creates peripheral nerve injury, resulting in morphological, physiological and chemical events in both the peripheral and central nervous system (Jensen and Nikolajsen, 1999). These changes are discussed below and presented in figure 2.3.

2.4.1 Peripheral mechanisms

When peripheral nerves are cut (as in amputation) the proximal nerve forms a terminal endbulb. In normal circumstances, fine processes or sprouts start growing out of the endbulb attempting to regenerate. However, in the case of amputation forward growth of the nerve is blocked causing the endbulbs and aborted sprouts to form a tangled mass called a neuroma (Devor, 2006). Neuromas cause ectopic discharge, a discharge which originates in the axonal endbulb, sprout, patch of dysmyelination or in the soma (cell body) and not the peripheral sensory ending (Flor, 2002). It occurs in Aβ, Aδ, C fibres and dorsal root ganglion cells (Devor, 2009) and may be due to dysregulation of the synthesis and / or function of ion channels.

Neuromas exhibit spontaneous activity (Dorsi *et al.*, 2008). Abnormal ectopic discharge occurs both in myelinated (A) and unmyelinated (C) axons but injured sensory axons are more likely to generate spontaneous ectopic activity than motor fibres (Devor, 2006). A fibres tend to fire earlier and in higher proportion than C fibres and the proportion of spontaneously active fibres after peripheral nerve injury are more than 80% in Aβ and Aδ fibres but only 0-30% in C fibres (Ossipov *et al.*, 2006). Outgrowing sprouts of neuromas become mechanically sensitive and can be detected by gentle tapping along the course of the damaged nerve (Melzack and Wall, 2008). In amputees, percussion of the stump or stump neuromas can induce stump pain and PLSd (Nystrom and Hagbarth, 1981). Neuroma sprouts are in an abnormal chemical environment and are not in contact with chemicals normally generated by their target tissue. Sprouts absorb marker chemicals and compounds which they are not usually in contact with and change their chemistry accordingly (Melzack and Wall, 2008). Metabolic and chemical factors can excite ectopic discharge and exacerbate pain (Devor, 2006). Temperature affects discharge rates of neuromas. In myelinated fibres, the rate of spontaneous discharge increases with warming and cooling suppresses firing. In non-myelinated axons the

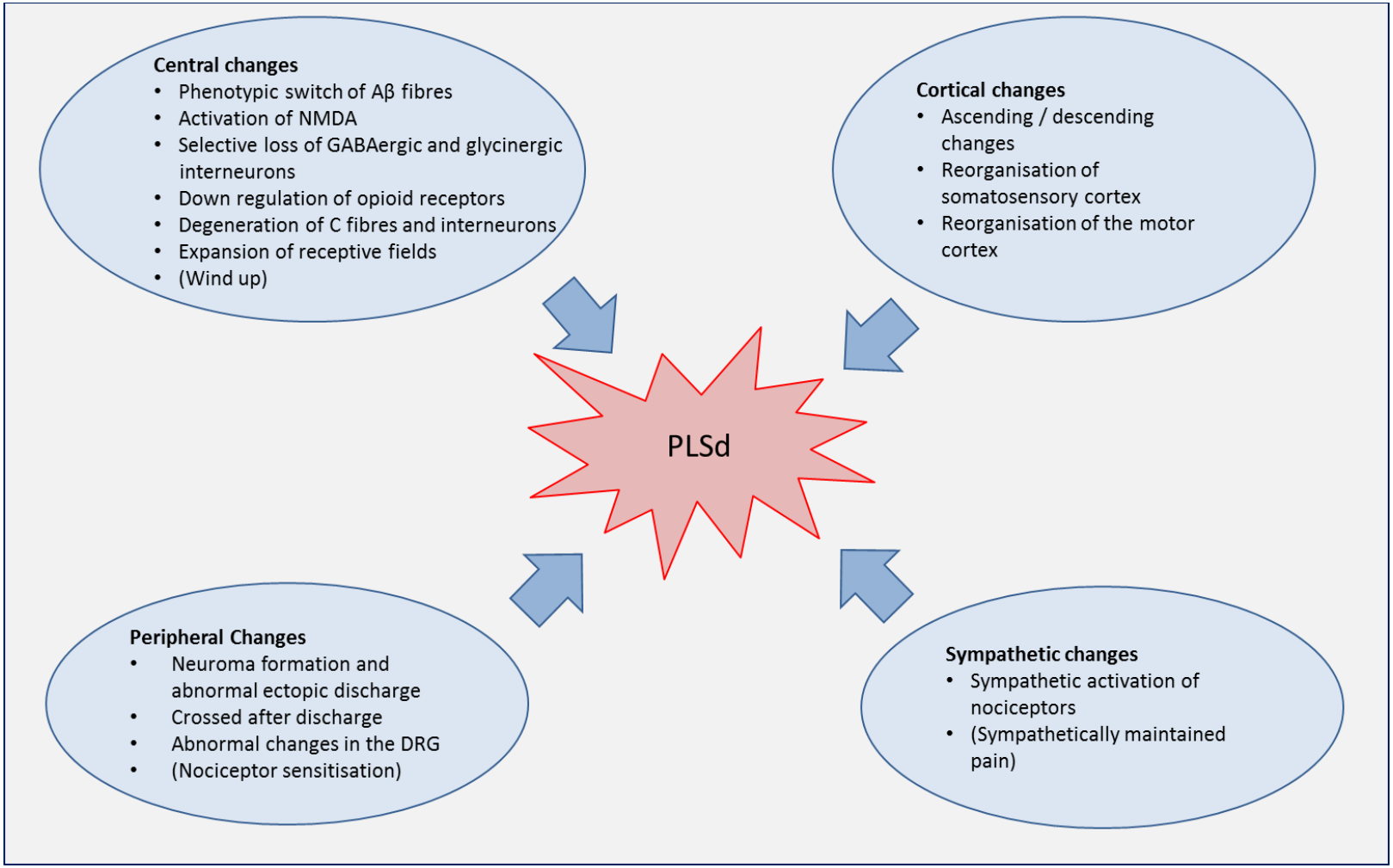
opposite occurs (Matzner and Devor, 1987).

PLSd can also be exacerbated by crossed after discharge (repetitive synchronous activity in primary afferents inducing firing in passive neighbours). This occurs early after nerve injury, does not rely on structural alterations (Attal and Bouhassira, 1999) and occurs only in spontaneously active neurons and the stimulated neighbour if they share the same dorsal root ganglion (Devor and Wall, 1990). Repetitive activity in afferent fibres excites non-stimulated neighbours as concentrations of the paracrine mediator build up progressively, winding up discharge rates in passive neighbours (Devor, 2006).

Sympathetic activation of nociceptors is another mechanism of PLSd and may explain why PLSd is exacerbated with emotional stress (Foell *et al.*, 2011). After amputation, damaged nerve membranes becomes sensitive to chemicals released by the sympathetic nervous system. Specifically, nerves develop alpha adrenergic receptors so that circulating catecholamines cause increased excitability (Melzack and Wall, 2008). Sympathetic blocks have been shown to give short term relief of PLSd (Cohen *et al.*, 2011) but studies assessing sympathectomy for neuropathic pain identify that there is a lack of high quality evidence supporting this technique (Straube *et al.*, 2010).

Post amputation, within the dorsal root ganglion, there is down regulation of some sodium channel expression and up regulation of others producing electrophysiological changes and causing them to fire spontaneously or at inappropriately high frequencies (Waxman, 1999). The dorsal root ganglion exhibits increased sensitivity to both mechanical and chemical stimulation, and crossed after discharge has been shown to occur, instigating the depolarisation of neighbouring neurons and contributing to neuropathic sensory abnormalities (Devor and Wall, 1990).

Figure 2.3 Mechanisms involved in phantom limb syndrome



2.4.2 Central mechanisms

Noxious stimuli due to nerve injury can induce central sensitisation, long-term changes in the synaptic responsiveness of neurones in the dorsal horn (Nikolajsen, 2012). Some changes affect the excitability of sensory and central neurons and are reversible (modulation). Other changes occur, which include long-lasting alterations in the expression of transmitters, receptors and ion channels, or in the structure, connectivity and survival of neurons (modification) (Woolf and Salter, 2000). Features of central sensitisation include; increased spontaneous activity of dorsal horn neurons, increased responsiveness to afferent input, after discharge, expansion of receptive fields, wind-up (Nikolajsen, 2012) a reduction in inhibitory processes and structural changes at the central nerve endings (Flor, 2002). Clinical manifestations of central sensitisation are hyperalgesia and allodynia (Nikolajsen, 2012).

Central sensitisation is usually triggered and maintained by nociceptive C fibre input (Devor, 2006). However, in traumatic neuropathy, ectopic spontaneous discharge is predominately found in the Aβ afferents. Normally Aδ and C fibres express substance P, a neuropeptide associated with inflammation and nociception (Nikolajsen, 2012) but following axotomy, Aβ fibres undergo a phenotypic switch and express new transmitters and neuromodulators including substance P and BDNF (brain-derived neurotrophic factor) (Latremoliere and Woolf, 2009). Release of substance P from injured Aβ fibres may enable them to transmit nociceptive information (Foell *et al.*, 2011) and consequences of this phenotypic switch include allodynia and pain due to spontaneous ectopic Aβ activity (Devor, 2006).

The main neurotransmitter in primary afferents is the excitatory amino acid glutamate. The principle receptor of this neurotransmitter in the dorsal horn is N-methyl-D-aspartate (NMDA) and amino-3-hydroxy-5-methylisoxazole-4 proprionic acid (AMPA) (Woolf and Mannion, 1999). Activation of nociceptors causes the release of glutamate which acts on AMPA but not NMDA (NMDA is closed at rest by a magnesium ion block and when glutamate binds to the receptor it does not activate an action potential). However, sustained barrage from the periphery causes a cascade of intracellular events, removes the magnesium block and results in NMDA's activation (Nikolajsen, 2012). Excessive stimulation of NMDA receptors leads to excitotoxicity and to destruction of

interneurons (Latremoliere and Woolf, 2009). This destruction of interneurons, which contain γ-aminobutyric acid (GABA) and glycine, causes central disinhibition leading to hyperexcitability of dorsal horn neurons (Attal and Bouhassira, 1999). Additionally, GABA receptors and opioid receptors are down regulated post peripheral nerve injury, causing further disinhibition of the dorsal horn with a loss of GABAergic and a reduction in glycinergic inhibitory currents (Woolf and Mannion, 1999).

Damage to primary afferents in peripheral nerves can induce anatomic changes in the dorsal horn and is associated with atrophic changes in central afferent terminals (Kohno *et al.*, 2003). Nerve injury results in degeneration of C fibres and their terminals in lamina II (Henry *et al.*, 2011) and it has been hypothesised that A fibres (including the large Aβ fibres) sprout from their deep dorsal horn laminar location up into the area of the spinal cord where the C fibres would normally terminate (laminae II) and make functional synaptic contacts (Woolf and Salter, 2000). However, this theory has been found to be unsatisfactory as the immune-histological marker (cholera toxin B subunit) thought to specifically label Aβ fibres has been found to also label C fibres after injury (Navarro *et al.*, 2007).

Studies have shown that central reorganisation after nerve injury produces changes in the receptive fields of the spinal cord. Each of the six laminae of the dorsal horn contain a map of the body surface and within this map each cell has its own receptive field (Melzack and Wall, 2008). Post nerve injury during peripheral regeneration there is a mismatch of the connections between the sensory receptors and afferent fibres with second-order neurones in the dorsal horn. This alters the somatotopy of the body representation at the spinal cord level and results in a loss of tactile discrimination and acuity (Navarro *et al.*, 2007).

2.4.3 Cortical mechanisms

Amputation alters neuronal activity in cortical and subcortical structures and PLSd is associated with alterations in the anterior cingulate, somatosensory and motor cortices, brainstem and thalamus (Foell *et al.*, 2011).

After peripheral nerve injury there is functional reorganisation of sensory and motor

systems and distortion of cortical maps (Navarro *et al.*, 2007). The most commonly studied cortical maps / virtual bodies are those in the S1 and S2 somatosensory cortices and in the primary motor cortex (M1) (Lotze and Moseley, 2007). However, there are other maps, and observations of plastic reorganisation have been observed in the primary visual cortex, the primary auditory cortex and in cognitive areas of the brain involved with language or attention (Navarro *et al.*, 2007).

Post amputation there is reorganisation of the somatosensory cortex surrounding the area representing the deafferented limb (Hsu and Cohen, 2013). The cortical field which is deprived of input shrinks and the receptive field becomes smaller. Adjacent representations from non-denervated parts of the body take over the cortical field (Navarro *et al.*, 2007). Similar effects are observed in the motor cortex. There is enlarged representation of cortical areas of muscles immediately proximal to the lesion and reduction / disappearance of motor maps of the denervated muscle (Navarro *et al.*, 2007). Imaging studies have shown that in human upper limb amputees the mouth invades into the hand representation (Pons *et al.*, 1991).

Cortical reorganisation causes abnormal circuitry and firing patterns that encode pain signals and cause pain (McCormick *et al.*, 2014). Also, the mismatch between motor commands and lack of proprioceptive and visual feedback may be perceived as pain (Ramachandran and Altschuler, 2009). The amount of cortical reorganisation in amputees varies with the amount of PLSd (Flor *et al.*, 1995). A significant relationship between the amount of cortical invasion and the amount of PLSd has been demonstrated, as has the relationship between the amount of cortical invasion and number of locations from which stimuli can cause referred phantom sensations (Knecht *et al.*, 1998). In a study by Karl *et al.* (2001) a correlation was seen between the magnitude of expansion into the receptive field and PLSd both in the somatosensory and motor cortex. Patients with PLSd had larger motor evoked potentials and a greater shift in representation in the somatosensory and motor cortex. Grüsser *et al.* (2001) found that changes in the somatosensory cortex were related to PLP, but not PLS, and Karl *et al.* (2004) found that amputees with PLSd showed a higher level of reorganisation in the sensorimotor cortex.

Two main mechanisms are involved in cortical and subcortical changes after

amputation; structural changes and unmasking of silent synaptic connections. Structural changes may occur over a period of time via axonal sprouting (Lotze and Moseley, 2007) and take weeks to months to occur (Elbert and Rockstroh, 2004). Changes which occur within minutes of deafferentation occur due to unmasking of previously silent / inactive synaptic connections. This unmasking may be due to increased excitatory neurotransmitter release, increased density of postsynaptic receptors, changes in membrane conductance, decreased inhibitory interactions or withdrawal of inhibitory projections. The most important cause of short–term plastic changes may be the removal of inhibition of excitatory synapses due to the reduction of GABAergic inhibition (Navarro *et al.*, 2007).

Summary of mechanisms involved in the pathology of PLSd

- PLSd is considered to be neuropathic pain.
- Although PLSd may originally be caused by peripheral nociceptive signals, over time central and cortical mechanisms are involved.
- Peripheral mechanisms involved include the formation of neuroma, abnormal ectopic discharge including spontaneous discharge, increased sensitivity to mechanical pressure and increased sensitivity to chemical and thermal stimuli.
- Crossed after discharge and abnormal changes in the dorsal root ganglion may contribute to PLSd.
- The sympathetic nervous system may contribute to PLSd due to sympathetic activation of nociceptors.
- Central changes involved include; a phenotypic switch of Aβ fibres, activation of NMDA, selective loss of GABAergic and glycinergic interneurons, down regulation of opioid receptors, degeneration of C fibres and interneurons, expansion of receptive fields and wind up.
- Cortical changes involved include cortical reorganisation possibly due to structural changes and unmasking of previously silent / inactive connections.

2.5 Qualitative review and meta-synthesis of amputees experience of phantom limb syndrome

A systematic search of qualitative papers was undertaken to gain insight into amputees' experience of PLSd. This was done to inform the author and aid the development of the project, through identifying if further qualitative research on amputees experience of PLSd was needed. As this review was undertaken to inform the qualitative descriptive study described in chapter 5, only qualitative papers were reviewed. ENTREQ guidelines were followed to ensure transparency of reporting (Tong *et al.*, 2012).

The search strategy aimed to be exhaustive. Six databases were searched initially in August 2013 and again in February 2015 with no limits set on dates of publication. Databases searched included; Pubmed, AMED, CINAHL, Medline, PsycINFO and ScienceDirect (from inception – February 2015). Search strategies are reported in Appendix 2.1. Papers were initially reviewed by examining the title and abstract. When it was unclear if the paper met the inclusion criteria or not, the full paper was read and the inclusion / exclusion criteria applied. Additionally, the reference sections of selected papers were checked for additional papers. Grey literature was not searched as the author wanted to identify literature which had been published in peer reviewed journals.

Inclusion criteria for studies were; (1) adults (≥ 18 years) who had undergone amputation and experienced PLSd in any context / setting, (2) studies involving a qualitative approach, (3) published in English, (4) published in a peer reviewed journal. Studies were excluded if they; (1) focused on the experience of amputation rather than PLSd, (2) focused on evaluation of or satisfaction with services, (3) included participants both with and without amputation, and information relating to those who had undergone amputation could not be clearly defined, (4) focused on quantitative findings when using MMR, (5) published before 1980 and (6) focused on phantoms other than of a limb such as phantom tooth pain and phantoms post mastectomy.

2.5.1 Appraising qualitative studies

Guidelines for appraising qualitative studies tend to view qualitative research as being

one type of approach, not acknowledging the diversity of methods (Daly *et al.*, 2007). Also, there is often discussion about the need for critical reflexivity in appraisal tools (Daly *et al.*, 2007). The consolidated criteria for reporting qualitative research (COREQ) was developed as a formal reporting checklist for the reporting of studies that use in-depth interviews and focus groups. It consists of three domains; research team and reflexivity, study design, and data analysis and reporting, and consists of 32 criteria (Tong *et al.*, 2007).

In this review COREQ was chosen over other appraisal tools due to its suitability for appraisal of studies using interviews and focus groups and its critical reflexivity. The critical appraisal skills program (CASP) is frequently used to appraise qualitative studies and was considered. However, as CASP only provides 10 criteria, of which two are screening criteria (CASP, 2013), COREQ was considered to provide a more detailed checklist. Also, COREQ was developed partly from CASP (Tong *et al.*, 2007). A rating system was developed by the author to score studies and evaluate the quality of the studies. This involved using a three-point system. 0 points were assigned when no justification or explanation was provided. 1 point was assigned where an incomplete justification or explanation had been provided and 2 points where the study had extensively justified or explained the issue under debate. The scores from all 32 items were totalled for each article allowing for a possible maximum score of 64. As a single numerical score provides limited information (Boland *et al.*, 2014) the COREQ check list was also provided to give further details about the quality of the studies. Appraisal was conducted independently by the author.

2.5.2 Data extraction and meta-synthesis

Data were extracted to preserve the context of the included studies. Data were extracted on the methodology, method used to collect data, data analysis technique, study aims, research setting, geographical location of the research, sample size, participant characteristics and research findings.

The researcher acknowledged the opinion that because qualitative research may involve different philosophical assumptions and is specific to the time, context and particular participants involved, it should not be synthesised. However, in this review the view

was taken that meta-synthesis could inform practice (Thomas and Harden 2008). Meta-synthesis was undertaken using thematic synthesis (Atkins *et al.*, 2008, Thomas and Harden, 2008). This approach was taken because thematic synthesis suited the aims of this meta-synthesis; to aggregate / summarise the identified qualitative data (Boland *et al.*, 2014) and because thematic synthesis is rigorous and transparent (Thomas and Harden, 2008). Thematic synthesis followed Thomas and Hardens, (2008) approach.

A priori it was decided that the meta-synthesis would be exhaustive and all identified papers would be included, regardless of their methodological quality or theoretical perspective. Findings were considered to be all text labelled as 'results' and data were only extracted from this section of included papers.

The computer-assisted qualitative data analysis software NVIVO 10 was used during synthesis. All papers were uploaded and inductively thematically coded, using a line by line approach. Codes could be structured hierarchically or be free codes. All data were coded and data could be categorised to more than one code. A code recode procedure was developed where the researcher recoded one paper one week after initial coding. Additionally a second coder also coded one paper to ensure consistency of interpretation and to establish whether additional levels of coding were needed. Post completion of coding, similarities and differences between codes was established and codes were grouped into descriptive themes. Analytical themes were drawn from the results. To aid fully synthesising the data "one sheet of paper" (OSOP) analysis was completed. This involved noting on a single piece of paper all issues captured under a code (Ziebland and McPherson, 2006).

2.5.3 Results of systematic search

The database search returned 254 studies (figure 2.4). Of these 149 did not meet the inclusion / exclusion criteria and 93 were duplicates. A total of 12 papers were screened through reading the full text, and of these, seven met the final inclusion criteria. Hand searches of the included studies reference list did not yield any additional papers.

Figure 2.4 Flow diagram of papers included in the qualitative literature review

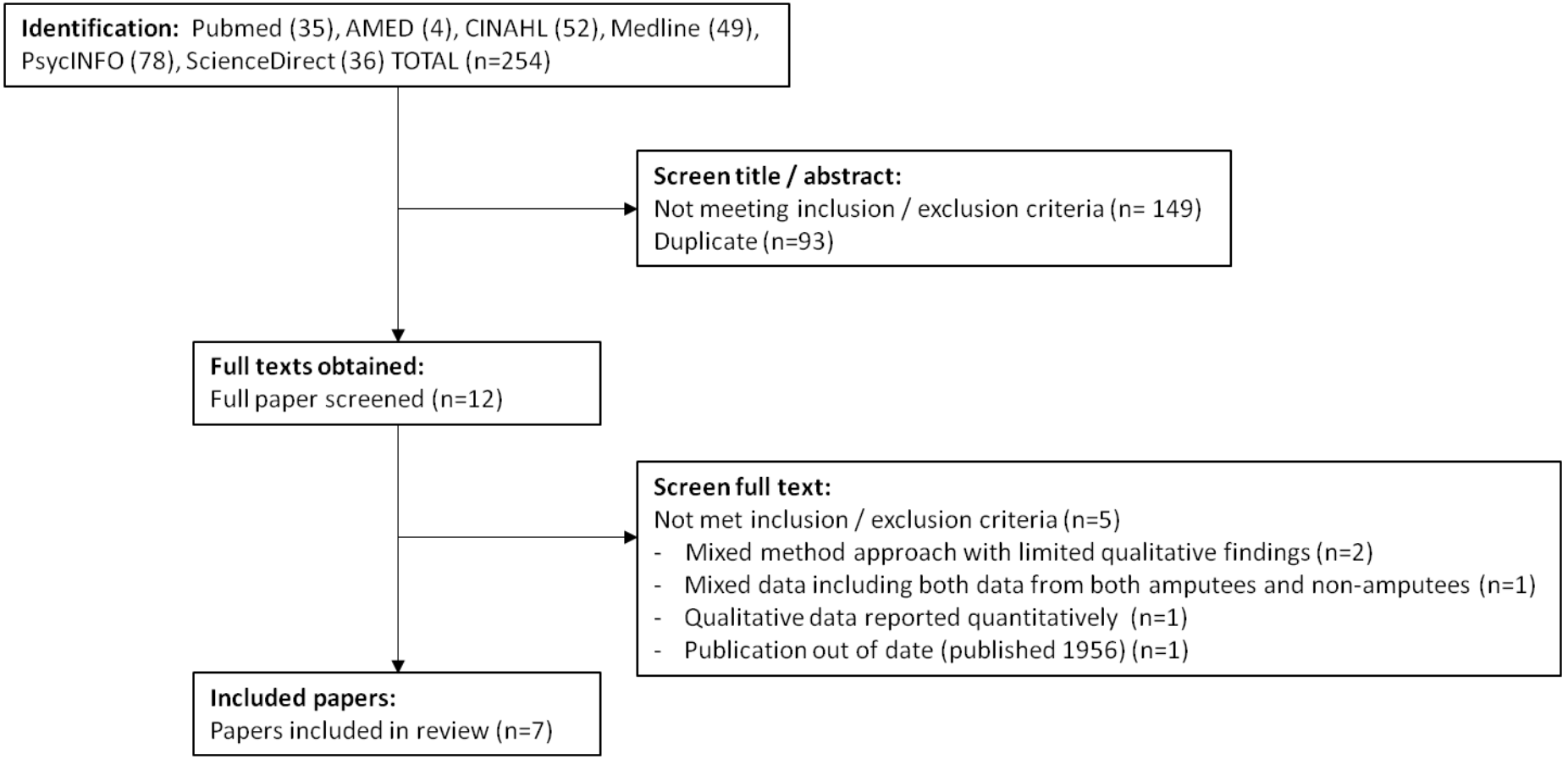


Table 2.1 provides a summary of characteristics of the seven qualitative studies identified. Studies were undertaken between 1982-2014 in countries including the UK, India, the Netherlands, Sweden and the USA. Studies were of different methodological design and three did not specify the methodology used. Six of the studies used interview methods to collect data and one used a focus group. The objective of all included studies was to examine / explore / study / describe the experience of PLSd. Two studies also explored amputees' perception and opinion on available information on PLSd. Sampling methods used included convenience sampling or consecutive cases. The UK and Dutch studies tended to include participants who had undergone amputation due to peripheral vascular disease. Of the studies completed in Sweden (same participants in each study) most had undergone amputation due to cancer, in India most were due to accidents and the USA study did not report on the reason for amputation. Three studies reported on lower limb amputees only. Time since amputation was not reported in one study and the others ranged from 1 month to 39 years. Four studies included participants of widely varying duration of time since amputation.

During the meta-synthesis, a total of 26 codes were identified. These were grouped into six descriptive themes and from these four analytical themes emerged. Analytical themes identified included; loss: both physical and mental, experiencing PLSd, attitude to PLSd and a need to know more. Amputees' opinions on improvement to information provided were not reported as this was not the aim of this review (to gain insight into amputees' experience of PLSd).

Table 2.1 Characteristics of studies included in the qualitative review

Paper / COREQ score	Country	Mthdoly / method / analysis	Research aims	Setting of data collect-ion	Sampling method (sample size)	Time since amputation	Reason for amputation	Level of amputation	Age at time of study, gender	Findings
Shukla *et al.* (1982) / 12	India	Phenomenology / interviews / U	To study phantom limb phenomena	MLB medical college, India	Consec cases (72)	U	Accidents (n=50) Osteosarcoma (n=7) Violent incidences (n=6) Burger's disease (n=3) Electric burns (n=3) Other (leprosy, madura foot, osteomyelitis) (n=3)	Upper limb (n=38) Lower limb (n=34)	10-30y (n=46) 30-50y (n=16) 50+y (n=10) M (n=68) F (n=4)	PLP was experienced by over $^{2}/_{3}$ of pts. PLSd was more common following amputation of the right arm. Nearly half of all PLSd developed within 24 hours, appearing earlier in lower limb amputees. Movements were felt by ¾ of cases and telescoping in nearly $^{2}/_{3}$ of pts. 31 pts dreamed their limbs were intact
Mortimer *et al.* (1998) / 24	UK / Scotland	U / interviews / U	To examine pts experiences of PLSd, their perception of relevant support and information received during rehabilitation	Central limb fitting service clinic	Conv (12)	<6m (n=4) 6m-1y (n=1) >1y (n=7)	PVD (n=8) Trauma (n=1) Other (n=3)	Below knee (n=8) Above knee (n=4)	30-49y (n=5) 50-69y (n=5) 70+y (n=2) M (n=9) F (n=3)	PLSd may affect quality of life and require strong medication. Information provided about PLSd is inconsistent and may also be insufficient

Paper / COREQ score	Country	Mthdoly / method / analysis	Research aims	Setting of data collect-ion	Sampling method (sample size)	Time since amputation	Reason for amputation	Level of amputation	Age at time of study, gender	Findings
Mortimer *et al.* (2002) / 30	UK / Scotland	U / focus groups / U	Explore the experiences of PLSd; Explore the experience and perceptions of information received on PLSd; Explore the perceptions and opinions about what should be told about PLSd and areas in need of development	Various unspec-ified locations	Conv (31)	Mean: 28m. Range: 6-117m	PVD (n=24) Trauma (n=3) Cancer (n=2) Osteomyelitis (n=2)	Below knee (n=24) Above knee (n=7)	30-49y (n=10) 50-69y (n=14) 70+y (n=7) M (n=18) F (n=13)	Information about PLSd does not meet amputees' needs. The timing and context of information provided is variable. Amputees require timely and adequate information about PLSd
Bosmans *et al.* (2007) / 22	Netherlands	U / interviews / U	Explore the impact of amputation and PLSd on the subjective wellbeing of amputees	Not stated	Consec cases (16)	1m-20y	PVD (n=8) Diabetes mellitus (n=6) Trauma (n=1) Infection (n=1)	Below knee (n=13) Above knee (n=3)	<41y (n=1) 41-60y (n=3) 61+y (n=12) M (n=11) F (n=5)	PLSd had a small impact on subjective wellbeing in most pts. However, unbearable PLSd was found to have a larger influence. This influence was less when pts had meaningful roles and activities in life

Paper / COREQ score	Country	Mthdoly / method / analysis	Research aims	Setting of data collect-ion	Sampling method (sample size)	Time since amputa tion	Reason for amputation	Level of amputation	Age at time of study, gender	Findings
Björkman *et al.* (2010)* / 29	Sweden	Narrative study / interviews / NA	Explore the ways pts describe and evaluate their PLSd when attempting to give meaning to their experience	Authors office or the pts home	Consec cases (28)	1m	Cancer (n=18) PVD (n=7) Trauma (n=3)	Limb amputation (n=20) Mastectom y (n=8)	18-45y (n=6) 45-65y (n=14) 65+y (n=8) M (n=12) F (n=16)	Pts need to be provided with information about PLSd. Health professionals need to listen to pts descriptions of PLSd, functional losses and life changes
Björkman *et al.* (2012)* / 26	Sweden	Narrative study / interviews / TCA	Describe how pts experienced and interpreted PLSd post amputation or mastectomy	Authors office or the pts home	Consec cases (28)	1m	Cancer (n=18) PVD (n=7) Trauma (n=3)	Limb amputation (n=20) Mastectom y (n=8)	18-45y (n=6) 45-65y (n=14) 65+y (n=8) M (n=12) F (n=16)	There is a need to observe the individual approach to PLSd. Experience and understanding of PLSd has sociocultural aspects

Paper / COREQ score	Country	Mthdoly / method / analysis	Research aims	Setting of data collect-ion	Sampling method (sample size)	Time since amputa tion	Reason for amputation	Level of amputation	Age at time of study, gender	Findings
Evans (2014) / 28	USA	DVS / interviews / CA	To identify the relative frequencies of *a priori* categories of PLSd; analyse descriptions for emerging categories; identify relative frequencies of emerging categories	Either over phone or at a location of the pts choosing	Purp, conv (52)	Mean: 7.1y Range: 0.5-39.0y	Not specified	Lower limb loss only (88.5%)	Mean age ± sd (52.5 ± 14.7y) M (71.2%)	Detailed descriptions of PLSd provide insight into the experience of this phenomenon

Key: PLP, phantom limb pain; PLSd, phantom limb syndrome; mthdoly, methodology; DVS, descriptive verbal survey; U, unspecified; NA, narrative analysis; TCA, thematic content analysis; CA, content analysis; PVD, peripheral vascular disease; m, months; y, years; M, males; F, females; pts, participant; consec, consecutive; conv, convenience; purp, purposive.

* The two studies were completed on the same set of participants

2.5.3.1 Theme 1: Loss: both physical and mental

Although this review only included papers which focused on PLSd and not amputation, papers described PLSd within the context of undergoing amputation, resulting in the emergence of this theme. The theme was included in the review for completeness and to give context to PLSd and describes emotions experienced and physically coping with the loss of a limb. Various emotions were expressed about the loss of a body part including feelings of being half a person, deep sadness, feeling hindered and anxious (Björkman *et al.*, 2010, Björkman *et al.*, 2012). There was also the feeling that only other amputees could understand what they were going through (Mortimer *et al.*, 2002). Alongside these emotions concerns were expressed about loss of mobility, coping and dependence.

> *"When I lost my leg I became very sad. I'm alone and how will I be able to cope when I've lost my leg. I'm very sad."* (Björkman *et al.*, 2010, p. 47)

However, this was not always the case in younger amputees who were more confident about their physical capabilities (Björkman *et al.*, 2010).

Amputees used coping strategies such as distraction to reduce the distress caused by loss of function, and rehabilitation and advances in prosthetic technology were considered important, offering a possibility to recapture former capacity (Björkman *et al.*, 2010). Loss of a body part meant changes to work, activities and living. Changes in living ranged from receiving aid from a partner or domestic help to having the home adapted or moving home (Bosmans *et al.*, 2007). Amputees who returned to work expressed satisfaction, but amputees missed skills such as walking, biking and driving a car. Most amputees had to look for new hobbies and found it difficult to live meaningfully (Bosmans *et al.*, 2007). Subjective wellbeing varied post amputation due to amputees viewing their ability to return to normal life differently (Bosmans *et al.*, 2007). Amputation generally positively affected relationships, with amputees spending more time with their partner and seeing more of children initially, but not later (Bosmans *et al.*, 2007).

2.5.3.2 Theme 2: Experiencing phantom limb syndrome

This theme comprised of three subthemes. The first, the course of PLSd, describes the onset, prevalence and course of PLSd and the effectiveness of different treatments. PLSd appeared within 24 hours of amputation in half of amputees and in a quarter between 24-48 hours (Shukla *et al.*, 1982). At the time of interview most participants reported having experienced PLP (Björkman *et al.*, 2010, Björkman *et al.*, 2012, Mortimer *et al.*, 1998, Mortimer *et al.*, 2002, Shukla *et al.*, 1982, Bosmans *et al.*, 2007) and PLP was often reported to occur in conjunction with PLS (Björkman *et al.*, 2010, Björkman *et al.*, 2012, Mortimer *et al.*, 1998, Shukla *et al.*, 1982). PLP or PLS alone was less common (Björkman *et al.*, 2010, Björkman *et al.*, 2012, Shukla *et al.*, 1982).

Although PLSd could reduce over time (Shukla *et al.*, 1982) generally this was not the case. PLSd did not seem to have a set pattern with some amputees reporting it faded over time, and others reporting it increased (Björkman *et al.*, 2010, Mortimer *et al.*, 1998). Intensity of pain did not correlate with time since amputation, but despite intensity not necessarily decreasing over time, frequency of PLSd could reduce (Mortimer *et al.*, 2002). Regardless of this unclear course, amputees were often confident that PLSd would either disappear or become manageable over time (Björkman *et al.*, 2010).

Amputees were usually positive about acute surgical pain management (Björkman *et al.*, 2012) but were less certain about treatment of PLSd. A number of different interventions were used including; pharmacological, transcutaneous electrical nerve stimulation (TENS), relaxation, massage, acupuncture and pain clinics, but these were usually not perceived as beneficial (Mortimer *et al.*, 1998). A desire for counselling was expressed (Mortimer *et al.*, 1998) as was the need for accessible long term support and information, preferably from someone in a similar situation.

> *"And it is going to have to be a counsellor with contact number... So then when you're in a position emotionally to think okay what was said about that aspect that you can phone up and say what was it you said or you can make an appointment."*(Mortimer *et al.*, 2002, p. 300)

> *"I would have liked to have been put in touch with somebody in a similar situation… nobody can tell you what you are going to go through unless [they've] been through it [themselves]."*(Mortimer *et al.*, 1998, p. 355)

The second subtheme, describing PLSd, describes the qualities of PLSd including frequency and intensity of symptoms and aggravating and easing factors. All amputees could distinguish between PLP, PLS and stump pain (Björkman *et al.*, 2010). PLSd was described descriptively in detail (Evans, 2014) using a combination of spatioexperiential descriptors, visual descriptors and descriptors involving actions or movements or embodying an object (Björkman *et al.*, 2012). The functioning body was used as a reference and PLSd was often described metaphorically (Björkman *et al.*, 2010).

> *"sometimes it stabs, you can feel that someone is digging into your Achilles tendon or someone is thrusting fire into the arch of your foot"*(Björkman *et al.*, 2010, p. 47)

Amputees considered PLP normal, and it was described openly as a real pain (Björkman *et al.*, 2010, Mortimer *et al.*, 2002). It could both be difficult to describe and described in exact detail (Björkman *et al.*, 2010). It usually presented distally (Mortimer *et al.*, 1998) as more than one sensation and could resemble a past experience (Mortimer *et al.*, 2002, Shukla *et al.*, 1982). It could vary in nature, causing a diverse range of descriptions (Mortimer *et al.*, 2002, Evans, 2014).

> *"But I do get maybe once or twice a week either a sharp stabbing pain or just a gripping sticking a needle in your leg and the toes in the vice feeling"*(Mortimer *et al.*, 2002, p. 296)

Those who had undergone mastectomy described the phantom less vividly and had difficulty in giving it form and location (Björkman *et al.*, 2010, Björkman *et al.*, 2012). Characteristics of PLP were identified by Mortimer *et al.* (2002), Shukla *et al.* (1982), Evans (2014) and Mortimer *et al.* (1998). A total of 29 different words were used to describe the characteristics of PLP, of which the most prevalent were severe and stabbing (figure 2.5).

Figure 2.5 Word cloud of the different characteristics of phantom limb pain

As with PLP, PLS was experienced vividly and often presented as itching, pricking, tingling or changes in temperature (Björkman *et al.*, 2010, Mortimer *et al.*, 1998, Evans, 2014). It was described as simple sensations (such as itching or tingling), complex sensations (feeling the limb), movement (which could be spontaneous or willed) and super added sensations (such as feeling ulcers or gout) (Mortimer *et al.*, 1998).

> *"for months before the amputation I had a toe nail which gave me a bit of trouble on one side it was ingrown a bit and I can still feel that most nights when I go to bed and lie down"*(Mortimer *et al.*, 2002, p. 297)

Although PLSd could be constant, it was often intermittent (Mortimer *et al.*, 2002, Shukla *et al.*, 1982, Evans, 2014) and described as, "pulsates/stabs real quick," "instantaneous zingers," "most are oscillating or shooting 3 seconds to 2 minutes apart," "can last for 30 seconds or couple hours," and "not a steady pain, but in waves." (Evans, 2014). Amputees who experienced constant PLSd experienced times of severe pain superimposed upon a dull ache (Shukla *et al.*, 1982). The intensity of PLSd was diverse and could vary from a twinge to severe pain, even within one amputee (Björkman *et al.*, 2010, Mortimer *et al.*, 1998, Mortimer *et al.*, 2002, Bosmans *et al.*, 2007).

> *"I have a lot of pain still, a lot of phantom pain...it gives a wee bit one time or another but other times it gets really terrible I can hardly bear it, the pain."*(Mortimer *et al.*, 2002, p. 295)

PLSd was aggravated through touching or approaching the stump, thinking about the consequences of amputation and through keeping the stump in one position (Shukla *et al.*, 1982). Symptoms were eased through distraction (Bosmans *et al.*, 2007) but amputees also felt unable to resolve their pain "feels like I want to rub it, but it is not there," (Evans, 2014).

The third sub-theme, other phantom experiences, describes kinetic and kinaesthetic experiences. Amputees experienced kinaesthetic sensations post amputation (Björkman *et al.*, 2010, Bosmans *et al.*, 2007, Shukla *et al.*, 1982) and adaptation to a new reality was a gradual process which took time (Björkman *et al.*, 2010). Kinaesthetic sensations usually faded over a period of weeks (Bosmans *et al.*, 2007) and some amputees reported telescoping (Shukla *et al.*, 1982). Some amputees dreamt they had normal limbs, but even within these dreams there was an awareness that they had undergone amputation (Shukla *et al.*, 1982).

> *"even in bed I stretch out my stump and I can feel my heel at the bottom where it should be but it's not."*(Mortimer *et al.*, 1998, p. 353)

Kinetically, phantom limbs behaved like the limb before it was detached (Björkman *et al.*, 2010). Movement could be willed, associated with stump movement or spontaneous (Mortimer *et al.*, 1998) and was not always under the amputees' control (Shukla *et al.*, 1982).

> *"Lying in bed the other day I thought 'I'm moving my toes'. But I didn't move anything because nothing's left. But I actually experienced it. It was strange"*(Björkman *et al.*, 2010, p. 46)

2.5.3.3 Theme 3: Attitude to phantom limb syndrome

This theme describes attitudes and emotions associated with PLSd. Both PLP and PLS evoked a range of emotions. Amputees felt unprepared for PLSd and were surprised at

the reality and the persistence of it (Mortimer *et al.*, 2002). It could be considered annoying (Björkman *et al.*, 2012) unpleasant (Shukla *et al.*, 1982) and bothersome, for example as the itch could not be itched (Evans, 2014). PLSd was also described as 'hard' in amputees from a mid-southern America culture, indicating a struggle or suffering (Evans, 2014).

Kinetic and kinaesthetic experience were considered stressful (incomprehensible and tiring) as there was nothing there to cause the sensation (Björkman *et al.*, 2010). They were also considered bizarre, fascinating, nasty, frustrating, a burden (Björkman *et al.*, 2010) and unpleasant (Shukla *et al.*, 1982).

Severity of PLSd did not correlate with amputees' subjective wellbeing and did not influence friendships (Bosmans *et al.*, 2007). However, although it was generally considered a low hindrance (Björkman *et al.*, 2012) it could be distressing (Björkman *et al.*, 2010) and disabling (Mortimer *et al.*, 1998).

> *"A few times every day it hurt so bad that I almost cried. Now it's like that just a few times every week. And it often happens when you're standing and waiting for something or waiting to pay in a shop."*(Björkman *et al.*, 2010, p. 47)

2.5.3.4 Theme 4: A need to know more

This theme describes amputees' knowledge and understanding of PLSd and the desire for further information. Amputees described PLSd in terms of previous experience and knowledge (Björkman *et al.*, 2012) using popular concepts and definitions (Björkman *et al.*, 2010). Some information about the established pain medical model was included in descriptions, including knowledge of complex interactions between the nervous system, spinal cord and brain (Björkman *et al.*, 2010) as well as awareness of a higher central nervous system process possibly of psychological origin. Amputees were uncertain of their knowledge, remarks were made without conviction and amputees felt unprepared for PLSd (Björkman *et al.*, 2012, Mortimer *et al.*, 1998).

Although some amputees considered being provided with information about PLSd unimportant (Bosmans *et al.*, 2007) generally a need to understand was expressed (Björkman *et al.*, 2010). However, although some described information provided on

PLSd as valuable (Björkman *et al.*, 2012) others were not satisfied (Mortimer *et al.*, 1998). Information was not always provided (Björkman *et al.*, 2012), did not always come from a professional and sometime was only available if requested (Mortimer *et al.*, 2002). A desire for more information was apparent (Mortimer *et al.*, 1998).

> *"It is just I feel that I would like to know the reason for phantom pain, apart from that various people had mentioned it and that it would happen, but if anyone could explain why we should have a phantom…"*(Mortimer *et al.*, 1998, p. 355)

2.5.4 Quality of reporting and limitations of the review

Completeness of reporting is illustrated in table 2.2. Across all studies COREQ rating was ≤30/64 suggesting poor reporting of all included studies. No studies reported on the research team and reflexivity other than to name the interviewer and only three studies fully described their methodological orientation (Björkman *et al.*, 2010, Evans, 2014, Björkman *et al.*, 2012). Although Shukla *et al.* (1982) reported their study as a phenomenological study, this could be debated as the sample size was large for this type of study (72 participants), data produced were not rich in detail and provided no participant quotations in the text. The numbers of participants who refused to participate or dropped out of studies were not reported in three papers (Bosmans *et al.*, 2007, Evans, 2014, Shukla *et al.*, 1982) and details of where data were collected and presence of non-participants was not described in the majority of studies. Two studies provided only minimal demographic details about participants (Björkman *et al.*, 2010, Evans, 2014) reducing the transferability of results. Only one study provided details of the interview topic guide (Bosmans *et al.*, 2007) and field notes were only reported to have been taken in two studies (Bosmans *et al.*, 2007, Mortimer *et al.*, 2002). In the study by Evans (2014) some interviews were conducted over the telephone and none were audio recorded. Details of data analysis was minimally and poorly reported in three of the studies (Mortimer *et al.*, 1998, Shukla *et al.*, 1982, Bosmans *et al.*, 2007) and data saturation was not discussed in any of the studies. Although studies usually presented themes clearly, only three papers presented participant quotations to illustrate findings (Mortimer *et al.*, 1998, Mortimer *et al.*, 2002, Björkman *et al.*, 2010).

Table 2.2 Consolidated criteria for reporting qualitative studies (COREQ) rating of studies included in the qualitative review

Article ID	Research team and reflexivity								Study design													Analysis and findings								
	1. Interviewer / facilitator	2. Credentials	3. Occupation	4. Gender	5. Experience and training	6. Relationship established	7. Participant knowledge of the interviewer	8. Interviewer characteristics	9. Methodological orientation and theory	10. Sampling	11. Method of approach	12. Sample size	13. Non-participation	14. Setting of data collection	15. Presence of non participants	16. Description of sample	17. Interview guide	18. Repeat interviews	19. Reporting of use or not of audio / visual recording	20. Field notes	21. Duration	22. Data saturation	23. Transcripts returned	24. Number of data coders	25. Description of coding tree	26. Derivation of themes	27. Software	28. Participant checking	29. Quotations presented	30. Data and findings consistent	31. Clarity of major themes	32. Clarity of minor themes
Shukla et al 1982	××	××	××	××	××	××	××	××	×✓	✓✓	××	✓✓	××	×✓	××	✓✓	××	×✓	××	××	××	××	××	××	××	××	××	××	×✓	×✓	×✓
Mortimer et al 1998	××	××	××	××	××	××	××	××	××	✓✓	✓✓	✓✓	✓✓	✓✓	××	✓✓	××	××	✓✓	××	××	××	××	××	××	××	✓✓	××	✓✓	✓✓	✓✓	✓✓
Mortimer et al 2002	××	××	××	××	××	××	××	××	××	✓✓	✓✓	✓✓	✓✓	×✓	✓✓	✓✓	××	××	✓✓	✓✓	××	××	××	×✓	××	✓✓	✓✓	××	✓✓	✓✓	✓✓	✓✓
Bosmans et al 2007	✓✓	××	××	××	××	××	××	××	××	✓✓	✓✓	✓✓	××	××	××	✓✓	✓✓	××	✓✓	✓✓	××	××	××	××	××	×✓	××	××	××	×✓	✓✓	✓✓
Bjorkman et al 2010	✓✓	××	××	××	××	××	××	××	✓✓	✓✓	✓✓	✓✓	✓✓	✓✓	××	×✓	××	××	✓✓	××	✓✓	××	××	✓✓	××	××	××	××	✓✓	✓✓	✓✓	✓✓
Bjorkman et al 2012	✓✓	××	××	××	××	××	××	××	✓✓	✓✓	××	✓✓	✓✓	✓✓	××	✓✓	××	××	✓✓	××	✓✓	××	××	××	××	✓✓	××	××	×✓	✓✓	×✓	✓✓
Evans 2014	✓✓	××	××	××	××	××	××	××	✓✓	✓✓	✓✓	✓✓	××	×✓	××	×✓	××	✓✓	✓✓	××	✓✓	××	××	✓✓	××	✓✓	××	××	×✓	✓✓	✓✓	×✓

Key:, not documented, ××; partially documented, ×✓; documented, ✓✓.

It is acknowledged that the rigour of this review was reduced through not having access to a research team and through only being conducted by one person (the author). Some of the studies were not typical to that seen in the UK. In the Björkman *et al.* (2010) and Björkman *et al.* (2012) study, the majority of participants had undergone amputation due to cancer and mastectomy participants were included in the study. In Shukla *et al.* (1982) study, trauma accounted for the majority of amputations. These populations are atypical to UK amputees who usually undergo amputation due to gangrene, atherosclerosis, infection or trauma (NHS, 2014). Additionally, cultural differences also made the majority of studies less transferable to the UK population, often no sampling strategy was employed to ensure specific participant characteristics were captured and time since amputation often varied hugely.

2.5.5 Conclusion

PLSd caused vivid symptoms which were considered annoying, unpleasant and bothersome. However, studies included in the review tended to be of poor reporting quality and / or not specific to lower limb amputees. This review suggested that no recent UK study has explored whether information provided to amputees about PLSd is adequate. Further studies are needed on a more homogenous and typical group of UK participants to explore amputees' experience of PLSd, the effect this condition has on quality of life and to discover if information provided to amputees about PLSd is adequate.

Summary of qualitative review and meta-synthesis

- Only seven qualitative studies were identified which reported on the experience of living with PLSd.
- These papers tended to be of poor reporting quality and only three specifically reported on lower limb amputees. Of these three papers amputees were interviewed at varying times post amputation.

2.6 Identifying the evidence base of research on the management of phantom limb syndrome: a review of systematic reviews

Although many treatment options are available for PLSd, including preventative interventions, pharmacological treatments and other adjunctive interventions, to date no recent systematic review has examined overall effectiveness of these treatments and reviews only exist on specific areas of treatment. These reviews are difficult to interpret as they often comprise of studies that include both participants with PLSd and participants with other painful conditions. Appraising all published reviews allowed for this evidence base to be summarised and compared (Smith *et al.*, 2011) and allowed for the author to establish if PLSd is well managed or if adjunctive treatments such as acupuncture could be beneficial. The aim of this review was to (1) identify available systematic reviews evaluating the effectiveness of interventions to prevent / treat PLSd (2) summarise the quantity and quality of these reviews (3) describe the characteristics of these reviews (4) identify gaps in research areas. Guidelines developed by Smith *et al.* (2011) were followed when completing this review.

The databases PubMed/MEDLINE, AMED and CINAHL were searched from inception to April 2015 using the terms 'phantom limb' or 'phantom pain' or 'chronic pain' and 'systematic review' or 'meta-analysis'. Additional search terms are listed in appendix 2.2. The author initially screened papers by examining the title and abstract. When it was unclear if the paper met the inclusion criteria or not, the full paper was read and the inclusion / exclusion criteria applied. Grey literature was not searched as the researcher wished to identify only reviews included in peer reviewed articles.

Inclusion criteria for reviews were (1) Participants; reviews which included adult amputees with any stage or intensity of PLP or PLS (2) Interventions; any intervention to prevent or treat PLSd, excluding acupuncture or transcutaneous electrical nerve stimulation (TENS) as the author carried out a systematic review of controlled trials on the effectiveness of these interventions for the treatment of PLSd (appendix 2.4) (3) Comparators; reviews which measured effectiveness of treatment by comparing the intervention to a placebo / sham treatment, no treatment or to usual care (4) Outcomes (primary); any form of pain measurement or patient reported improvement (5) Study design; quantitative systematic reviews with individual studies of any study design (6)

Language; English language publications, (7) Date; published during or after 2000. Exclusion criteria for reviews were; < 10% of studies included in a systematic review were on participants with PLSd.

Included reviews were quality appraised and the quality and strength of evidence influenced conclusions drawn in this review. More than 24 instruments exist which assess the quality of systematic reviews (Shea *et al.*, 2007). A Measurement Tool to Assess Systematic Reviews (AMSTAR) was developed through building on the empirical data of previous assessment tools and through utilisation of expert opinion. It measures 11 components and was used as it has been shown to have good reliability and convergent validity (Shea *et al.*, 2007).

A summary (table 2.3) was developed by the author providing details of the scope of the included reviews and data were extracted on; review year, review aim, search strategy, total number of included studies and number of included studies specifically related to amputees with PLSd and AMSTAR score. Descriptive characteristics of included reviews were extracted on; population, timing of intervention, type of intervention, control, outcomes relevant to measuring changes in pain or patient reported improvement, results of the review and whether the review reported adverse events. This data is included in appendix 2.3.

2.6.1 Data synthesis

Data were interpreted through noting whether individual reviews reported positive, inconclusive or negative results, through the number of amputees with PLSd included in each review and through quality appraisal scores. During data synthesis, because some reviews included the same studies, duplicate studies were removed to allow for the true number of studies undertaken on the treatment of PLSd to be determined. A qualitative description / narrative summary of the reviews, grouped by treatment type was provided.

A meta-analysis was not undertaken as data from individual studies should not be used more than once and overcoming this would require unpicking each of the included reviews and subsequent combination of results (Smith *et al.*, 2011). This was considered

too time-consuming and complex for this review.

2.6.2 Results

The database search yielded a total of 1242 citations of which 160 were duplicates. Of the initially screened papers 1043 did not fit the inclusion / exclusion criteria. A total of 39 systematic review papers were screened through reading the full text and of these 25 were excluded because they did not include studies on PLSd, did not describe participant characteristics, did not evaluate change in PLSd and studies included on PLSd were < 10% of the total number of studies. A total of 14 systematic review papers were included in the final review (figure 2.6). These included 45 individual studies on PLSd (25 were duplicates and 2 not relevant as they evaluated TENS) of which 21 were well powered RCTs (level 2 evidence), 18 retrospective studies, open-label trials or pilot studies (level 3 evidence) and 6 anecdotes, case reports or clinical experience (level 4 evidence).

Table 2.3 provides a summary of the included studies and overall AMSTAR score (calculated using http://amstar.ca/Amstar_Checklist.php) and appendix 2.3 descriptive characteristics of the included studies, grouped by the type of intervention.

Figure 2.6 Flow diagram of studies included in the review of systematic reviews

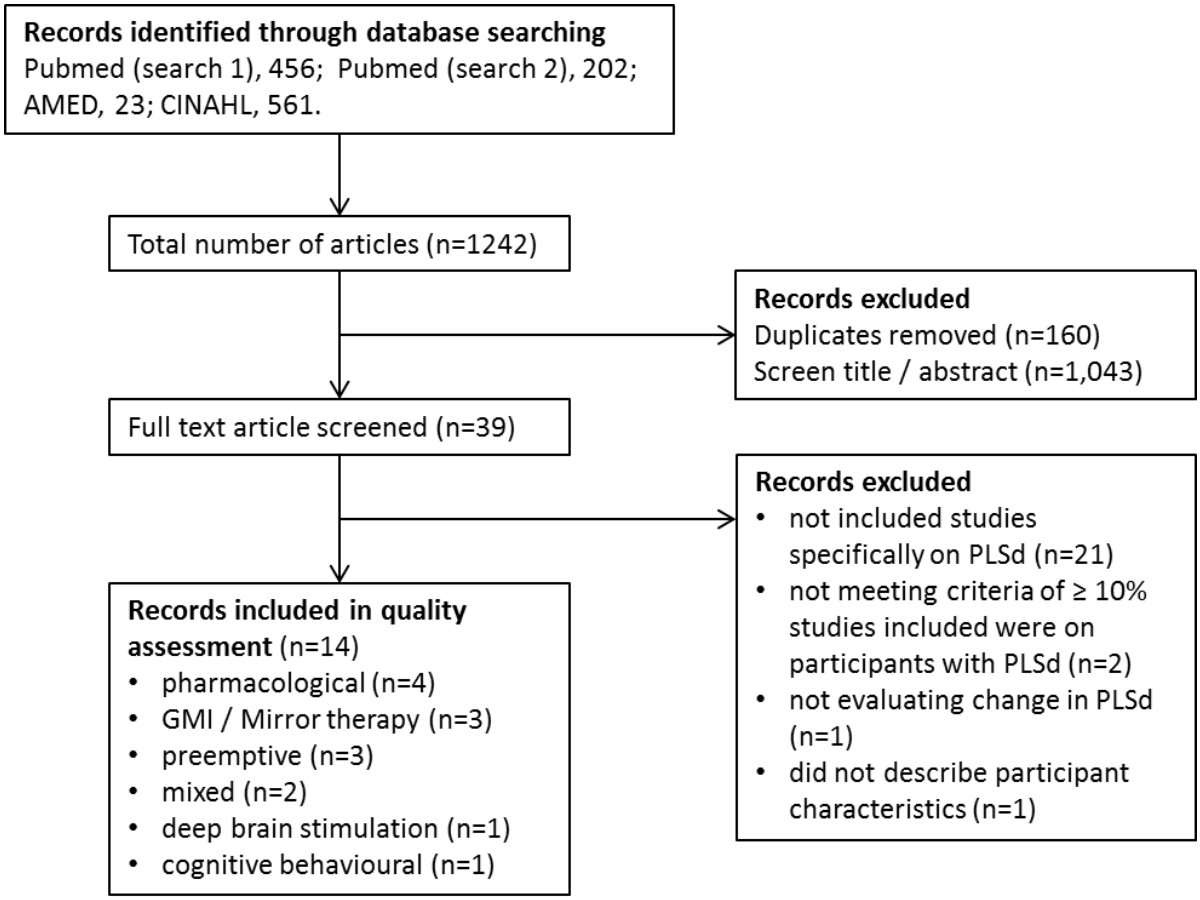


Table 2.3 Summary table of scope of papers included in review of systematic reviews

Review year	Study aim	Search strategy (year searched up to)	Total number of included studies (amputation specific)	AMSTAR score
Pre-emptive interventions				
Andreae and Andreae (2012)	To compare local anaesthetics and regional anaesthesia versus conventional analgesia for the prevention of persistent pain 6-12 months after surgery	Cochrane Central Register of Controlled Trials, PubMed, EMBASE, CINAHL (2012). Full search strategy provided. No language restrictions.	23(4); All RCT's.	11/11
Chaparro *et al.* *(* 2013)	To evaluate the efficacy of systemic drugs for the prevention of chronic pain after surgery by examining the proportion of patients reporting pain ≥ 3m after surgery and to examine the safety of these drugs.	Cochrane Central Register of Controlled Trials, Medline, EMBASE (2013). Full search strategy provided. Language restrictions not reported.	40(4); All RCT's.	9/11
Ypsilantis and Tang (2010)	To evaluate the potential effect of pre-emptive analgesia on the prevention of chronic pain after lower limb amputation due to critical ischemia.	MEDLINE, CINHAL, OVID, EMBASE, Cochrane Collaboration Library (2009). Full search strategy not provided. Search restricted to English language.	11(11); RCT (7), CCS (2), POCS (2).	3/11
Mixed interventions				
Humble *et al.* (2015)	To examine the impact of specific interventions on the management of perioperative pain and associated chronic pain.	MEDLINE, EMBASE and Cochrane Library (2014). Full search strategy not provided. Language restrictions not reported.	32(5); All RCT's	4/11
Halbert *et al.* (2002)	To determine the optimal management of PLP in the preoperative and postoperative phase of amputation.	MEDLINE (1999). Full search strategy not provided. Search restricted to English language.	12(12); RCT (3), NRCT (4), CS (1), RXO (3), XO (1).	4/11
Pharmacological interventions				
Abbas (2012)	To evaluate the effectiveness of gabapentin in adults with PLP	PubMed (2012). Full search strategy not provided. Search restricted to English language.	3(3); RCT (3) of which two were XO design.	1/11
Alviar *et al.* (2011)	To summarise the effectiveness of pharmacologic interventions for treating PLP.	Cochrane Pain Palliative and Supportive Care Review Group Trials Register, Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE (2011). Full search strategy provided. No language restrictions.	13(13); RCT (10), QRCT (3) of which 10 were XO design.	8/11

Review year	Study aim	Search strategy (year searched up to)	Total number of included studies (amputation specific)	AMSTAR score
Fang *et al.* (2013)	To review the mechanisms and current application of pharmacological interventions for PLP.	MEDLINE, PubMed, Index of Chinese Language Literature (2011). Full search strategy not provided. Search restricted to English and Chinese language.	96(96); study design not specified.	1/11
McCormick *et al.* (2014)	To review the evidence based pharmacotherapy for PLP in the context of understanding the patho-physiology PLP.	PubMed, EMBASE, Scopus and the Cochrane Central Register of Controlled Trials (2013). Full search strategy not provided. Language restrictions not reported.	Not specified.	4/11
Deep brain stimulation				
Bittar *et al.* (2005)	To examine deep brain stimulation for nociceptive and neuropathic pain.	MEDLINE, EMBASE (2003). Full search strategy not provided. No language restrictions.	6(not specified); study design not specified.	2/11
Graded motor imagery (GMI) / Mirror therapy				
Bowering *et al.* (2013)	To synthesize all available literature on the efficacy of GMI or any of its three components on chronic pain.	MEDLINE, EMBASE, CINAHL, Scopus, Academic Search Premier, Web of Science, Allied and Complementary Medicine, PubMed, Cochrane Collaboration, PEDro (2012). Full search strategy provided. Search restricted to English language.	6(2); All RCT's.	10/11
Rothgangel *et al.* (2011)	Evaluate the clinical aspects of mirror therapy after stroke, PLP and CRPS.	PubMed/MEDLINE, CINAHL, EMBASE, PsycINFO, PEDro, RehabTrials, Rehadat, DIMDI, Cochrane Database of Controlled Trials (2010). Full search strategy not provided. Search restricted to English, German, French and Dutch language.	21(5); RCT (10) of which 4 were XO design, PS (7), SCS (4). Amputation specific RCT (2), PS (1), SCS (2).	8/11
Timms and Carus 2015	To explore and discuss the current evidence assessing the efficacy of mirror therapy to treat PLP post amputation.	PubMed, AMED, CINAHL, Google Scholar (2013). Full search strategy not provided. Search restricted to English language.	7(7); RCT (2), PS (3), SCS (2).	4/11
Cognitive and behavioural interventions				
Wetering *et al.* (2010)	To evaluate the effectiveness of cognitive and behavioural interventions for the management of chronic neuropathic pain	Cochrane Library, PubMed/MEDLNE, EMBASE, CINAHL, psycINFO (2008). Full search strategy provided. Search restricted to English language.	14(6); RCT (3), NRCT (3), PS (7), TSA (1). PLP specific RCT (1), PS (4), TSA (1).	8/11

KEY: RCT, randomised controlled trial; CCS, case-controlled study; POCS, prospective observational cohort study; CS, cohort study; RXO, random cross-over study; XO, cross over; QRCT, quasi-randomised controlled trial; NRCT, non-randomised controlled trial; PS, patient series; SCS, single case study; TSA, time series analysis; m, month; PLP, phantom limb pain; CRPS, complex regional pain syndrome; GMI, graded motor imagery.

2.6.2.1 Pre-emptive interventions

Three reviews of which two were of high quality (scored ≥ 9/11 AMSTAR score), totalling 74 studies (70 RCTs) reported mixed results and inconclusive results. Of the included studies only 14 specifically reported on PLSd (9 level 2, and 5 level 3).

Evidence for the use of local or regional anaesthetics for the prevention of PLSd was found to be inconclusive in both reviews evaluating this (Andreae and Andreae, 2012, Ypsilantis and Tang, 2010). Systemic perioperative ketamine was recommended if delivered for more than 24 hours, but other systemic interventions such as gabapentin and pregabalin were found to be ineffective (Chaparro *et al.*, 2013). However, although Chaparro *et al.* (2013) high quality review reported favourably towards ketamine, of the included ketamine studies in this review, only one evaluated amputation / PLSd. This study of 45 lower limb amputees found at six months the incidence of PLSd in the ketamine group was 47% and in the control group 71%. This was not statistically significant and of note there was a significant proportion of missing outcome data; 14 participants (31%) at this time point (Hayes *et al.*, 2004). It was not possible to determine the likelihood or type of adverse events from pre-emptive interventions as reporting in this area was minimal.

2.6.2.2 Mixed interventions

Two reviews, both of which were of poor quality, totalling 44 studies (35 RCTs) reported inconclusive and conflicting results compared to reviews specifically evaluating pre-emptive or pharmacological interventions (Humble *et al.*, 2015, Halbert *et al.*, 2002). Of the included studies, 16 reported specifically on PLSd (8 level 2 and 8 level 3). Of these, 9 were studies included in the reviews on pre-emptive interventions (section 2.6.2.1), two were on TENS (not covered in this review), two were included in the reviews on pharmacological interventions (section 2.6.2.3), one had been excluded from a high quality review on pharmacological interventions (Alviar *et al.*, 2011) as PLSd was not established and two evaluated alternative non-pharmacological interventions (farabloc and vibratory stimulation). Due to the high duplication of studies included in these two papers with other papers included in this review and due to their poor quality, findings from other better quality papers were taken over these papers findings.

The two studies evaluating alternative non-pharmacological interventions were not included elsewhere in this review. Neither provided robust evidence in favour of their intervention. One study on farablock (a stump liner which shields nerve endings from external electromagnetic fields) reported favourable outcomes but was of poor methodological quality including no details on sample size calculation, randomisation, allocation concealment, methods of statistical analysis, duration of time wearing farablock or duration of washout period (Conine *et al.*, 1993). The study on vibratory stimulation suffered a high number of participants (71%) stopping treatment because it was ineffective, experiencing more pain or because pain was difficult to tolerate (Lundeberg, 1985).

2.6.2.3 Pharmacological interventions

Four reviews of which only one was of high quality, totalling at least 112 studies (at least 13 RCTs) generally reported inconclusive results. Of the included studies, of the ones the author could trace all reported specifically on PLSd. Of these 14 studies 11 were level 2 (but one of these evaluated pre-emptive treatment) and 3 level 3. It was not possible to assess the levels of evidence of the other studies as their citations and characteristics were not reported (Fang *et al.*, 2013, McCormick *et al.*, 2014). Of the two reviews which provided details of their included studies, the RCTs included in Abbass (2012) paper were identified in Alviar *et al.* (2011) review.

McCormick *et al.* (2014) low quality review reported PO morphine may provide intermediate to long term treatment effects, but this was based on the findings from one study of 12 participants. Two reviews (of high and low quality) reported morphine and ketamine may provide short term analgesic efficacy (Alviar *et al.*, 2011, McCormick *et al.*, 2014) but morphine findings were based only on two cross-over studies. Although Alviar *et al.* (2011) reported amitriptyline to be ineffective, this was based on the findings of one study of 39 participants. The effectiveness of gabapentin was conflicting. However, some gabapentin studies may have reported negative results due to small sample sizes, insufficient dosage and short duration of active treatment. Recommended maximum daily dosage of gabapentin for the treatment of neuropathic pain is 3600mg over an 8-10 weeks trial period (Abbass, 2012) but in the three identified trials two used dosages of 2400mg, two ran for 6 weeks and one 30 days. The reviews suggest

morphine and ketamine may cause moderate to severe adverse events whereas gabapentin may not cause adverse events.

2.6.2.4 Deep brain stimulation

One low quality review, including 6 studies, reported positive results for well selected participants. Of the included studies all were level 4 level of evidence and in total only 9 of 424 participants had PLSd and stump pain (Bittar *et al.*, 2005). Results of this review therefore should not be used to recommend treatment for amputees with PLSd.

A systematic review excluded from this review, as < 10% of studies included in the review were on participants with PLSd, reported negatively for using non-invasive brain stimulation techniques for chronic pain. Although this study only included 2/56 studies on PLSd, it was a high quality review and included only randomised and quasi-randomised studies, suggesting this technique may not be effective for treating chronic pain / chronic PLSd (O'Connell *et al.*, 2014).

2.6.2.5 Graded motor imagery / mirror therapy

Three reviews of which two were high quality (Bowering *et al.*, 2013, Rothgangel *et al.*, 2011) , and one low quality (Timms and Carus, 2015) totalling 34 studies (18 RCTs) generally reported positive results for GMI and its components (except mental imagery). Of the included studies only 10 reported specifically on PLSd (3 RCTs) of which 1 was level 2, 3 level 3 and 6 level 4.

Of the three RCTs reporting specifically on PLSd, two reported on mirror therapy. Chan *et al.* (2007) randomly assigned 22 participants to four weeks (15 minutes daily) of mirror therapy, mental visualisation or a covered mirror control. Pain intensity and number of pain episodes decreased in the mirror group (mean-24mm on a 100mm visual analogue scale) and pain intensity changes were found to be significant compared to the other two groups. However, no information was given on sample size calculation, method of randomisation, allocation concealment, on the participants who dropped out (18%) and minimal information was given about how the pain scale was used. Additionally participants were recruited soon after amputation so the trial did not include participants with chronic pain. Brodie *et al.* (2007) investigated if viewing a

virtual limb affected the experience of a phantom limb. 80 participants were recruited of which 43 (n=21 mirror, n=22 control) had PLSd at time of intervention. Both the mirror group and control group (who attempted to move the phantom limb at the same time as moving the intact limb) experienced significant attenuation of sensations and pain suggesting mirror therapy added no benefit to treating PLSd. However, the trial consisted of a one off intervention and assessed immediate changes in PLSd only so did not provide evidence on the effectiveness of a course of mirror therapy or its long term effectiveness. The third RCT reported on GMI. This single blind RCT with adequate sample size (n=51) assessed the effect of six weeks of intervention on participants with chronic regional pain syndrome (CRPS) type I, brachial avulsion injury and amputation related PLSd. Results were significantly positive both at reducing pain intensity and increasing function at six months for the treatment group compared to the control. However, of the sample only 9 were amputees (Moseley, 2006).

Although adverse events were not reported for mirror therapy in the included reviews, they have been reported elsewhere in amputees undergoing mirror therapy 20-30 days post amputation (Casale *et al.*, 2009). One review suggested GMI may increase pain.

2.6.2.6 Cognitive behavioural interventions

One high quality review of 14 studies (3 RCTs) of which 6 involved PLSd (1 level 2, 5 level 3) reported inconclusive findings due to the methodological quality of included studies (Wetering *et al.*, 2010). Of the studies evaluating PLSd, only one was a RCT (Brodie *et al.*, 2007). This has been described above (section 2.6.2.5).

2.6.3 Quality and reporting of included reviews and study limitations

The included reviews were of mixed methodological quality. A total of six scored ≥8 and eight scored ≤4 of a possible 11 AMSTAR score (table 2.4). Of the reviews which scored ≥8, the research question was clearly defined and study design was usually defined in PICO terms (population, intervention, comparator, outcome). At least two independent data extractors were always involved and a comprehensive literature search performed (but the specific search strategy was not always provided). Grey literature was not always searched and excluded studies were sometimes only documented in the

Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram. Characteristics of the included studies were always provided as was the scientific quality of these studies. Not all studies completed a meta-analysis due to the heterogeneity of included studies and publication bias was only considered for assessment in one paper.

Of the reviews scoring ≤4, none defined the research question in PICO terms and most did not report if there was a duplicate study selector and data extractor. Four of the studies did not perform a comprehensive literature search in terms of number of electronic sources used or reviewing reference lists. Grey literature was never searched or a list of excluded studies provided. The characteristics of the included studies were not provided in one paper and the scientific quality of included studies only appraised in two of the papers. None of the studies attempted to perform a meta-analysis or assess for publication bias.

A limitation of this review was the use of just one data extractor and quality assessment evaluator. Many included reviews only included limited data on PLSd and the quality of these reviews was sometimes poor. Studies included in reviews on the treatment of PLSd were few and often of poor methodological quality making it hard to determine if effective interventions exist. Included studies were not individually quality appraised and this may have led to an exaggerated number of level 2 studies being identified in this review. Quality appraisal may cause some level 2 studies to be considered level 3.

Table 2.4 AMSTAR assessment of methodological quality of papers included in the review of systematic reviews

	Was an 'a priori' design provided?	Was there duplicate study selection and data extraction?	Was a comprehensive literature search performed?	Was the status of publication (i.e. grey literature) used as an inclusion criteria?	Was a list of studies (included and excluded) provided?	Were the characteristics of the included studies provided?	Was the scientific quality of the included studies assessed and documented?	Was the scientific quality of the included studies used appropriately in formulating conclusions?	Were the methods used to combine the findings of studies appropriate?	Was the likelihood of publication bias assessed?	Was the conflict of interest included?
Andrea and Andrea (2012)	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Chaparro et al. (2013)	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y
Ypsilantis and Tang (2010)	N	CA	Y	N	N	Y	N	Y	NA	N	N
Humble, Dalton and Li (2015)	N	Y	Y	N	N	Y	N	N	NA	N	Y
Halbert, Crotty and Cameron (2002)	N	Y	N	N	N	Y	Y	Y	NA	N	N
Abbas (2012)	N	CA	N	N	N	Y	N	N	NA	N	N
Alviar, Hale and Dungca (2011)	Y	Y	Y	N	Y	Y	Y	Y	NA	N	Y
Fang et al. (2013)	N	CA	N	N	N	N	N	N	NA	N	Y
McCormick et al. (2014)	N	CA	Y	N	N	Y	N	Y	NA	N	Y
Bittar et al. (2005)	N	CA	Y	N	N	Y	N	N	NA	N	N
Bowering et al. (2013)	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y
Rothgangel, Braun and Beurskens (2011)	Y	Y	Y	N	Y	Y	Y	Y	NA	N	Y
Timms and Carus 2015	N	CA	N	N	N	Y	Y	Y	NA	N	Y
van de Wetering et al. (2010)	N	Y	Y	N	Y	Y	Y	Y	Y	N	Y

Key: Y, yes; N, no; CA, can't answer; NA, not applicable.

2.6.4 Conclusion

Evidence does not support the use of pre-emptive interventions. Pharmacological interventions may be effective for treating PLSd but studies are limited. Morphine and ketamine may be effective but risk moderate to severe adverse events. Gabapentin does not cause adverse events but further studies are needed to evaluate its effectiveness. Further studies are needed before confirming that amitriptyline should not be used to treat PLSd. Deep brain stimulation is not beneficial for chronic pain. Evidence on the effectiveness of GMI and mirror therapy is limited but preliminary findings suggest positive results. Further high quality, fully powered studies are needed to determine definitive interventions for PLSd.

These findings confirm that at present, evidence supporting interventions for PLSd are limited and that there is a need for high quality studies evaluating the effectiveness of both pharmacological and adjunctive interventions.

Summary of review of systematic reviews

- A total of 14 reviews were included in this review of reviews, which included 45 relevant studies on the treatment of PLSd.
- Of these studies only 21 were graded level 2. This may be a high estimate, and may be less if these studies were individually quality appraised.
- Of the included reviews, interventions were heterogeneous assessing pre-emptive interventions, mixed interventions, pharmacological interventions, deep brain stimulation, GMI / mirror therapy and cognitive behavioural interventions.
- Evidence did not support the use of pre-emptive interventions. Gabapentin, morphine and ketamine may be effective but further studies are needed. Ketamine and morphine may cause moderate to severe adverse events. Deep brain stimulation appears to be ineffective. GMI and mirror therapy may be effective but further high quality studies are needed before this can be determined.
- At present no intervention can be definitively considered effective for treating amputees with PLSd.

2.7 Identifying the evidence base of research on acupuncture for the treatment of phantom limb syndrome

A systematic review was undertaken in 2013 in collaboration with Chinese and South Korean colleagues to identify the evidence base of research on acupuncture for the treatment of PLSd. This was in keeping with the theoretical framework of the project (Chapter 3) and was undertaken as a preparatory step in the development of an acupuncture protocol for the treatment of PLSd which could be used in a definitive multi-centred RCT trial. As the systematic review was done in collaboration with colleagues and is not all the author's own work it has not been reported in this thesis but the publication is included in appendix 2.4.

In brief the systematic review included English, Chinese and Korean databases and explored the clinical effectiveness, cost effectiveness and adverse effects of acupuncture and TENS for the treatment of PLSd. Literature searches were carried out using 18 databases from inception to Feb 2013 (6 English, 4 Chinese and 8 Korean) using the terms 'phantom limb' or 'traumatic amputation' AND 'acupuncture' or 'TENS' Quality appraisal was established using the consolidated Standards of Reporting Trials (CONSORT) and Transparent Reporting of Evaluation with Nonrandomised Designs (TREND) checklists. Risk of bias was assessed using the Cochrane Collaboration tool for RCTs and Downs and Black for non-randomised controlled trials.

Of 1005 potentially relevant studies, a total of five were identified and included in the systematic review (four non-randomised controlled trials and one RCT). Of these two non-randomised controlled trials evaluated the effectiveness of acupuncture (table 2.5). Both reported acupuncture significantly reduced PLSd but both were also deemed to have a high risk of bias and low methodological quality. Neither study provided information on adverse effects or cost effectiveness and no specific outcome measures or treatment guidelines could be drawn from the studies.

The literature search was updated in June 2015 by the author (English databases only) using the same search terms as those used in the original review. No further controlled trials were identified (figure 2.7).

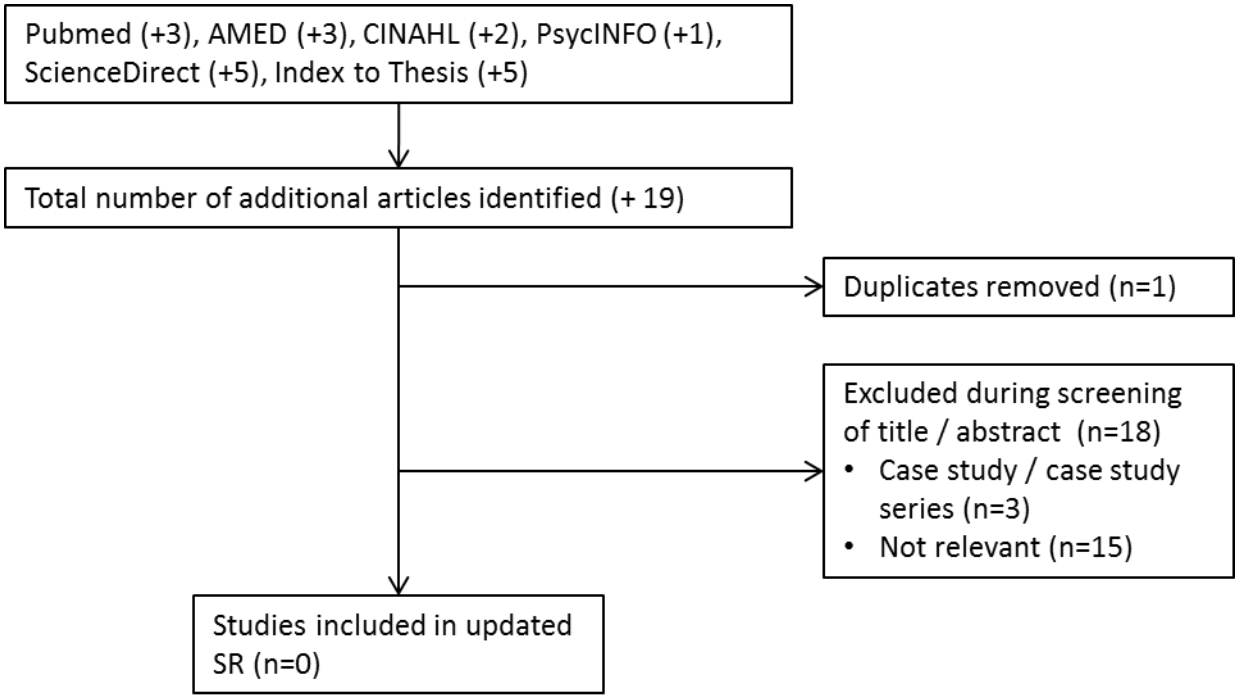
Table 2.5 Data extracted from controlled trials assessing effectiveness of acupuncture intervention for treating phantom limb syndrome

Study	Country	Study type; (sample size)	Reason for amputation; time since amputation; type of amputation; participant age	Intervention	Control	Outcomes	Long term follow up
Yang *et al.* (2010) (Chinese)	China	NRCT; (n=44)	Trauma; N/A; UL=6, LL=38 including 4 cases in both sides; 14-55y, median 41.5y	Acupuncture for 20 mins. Treatment 1X daily + rehabilitation programme. 5 treatments per w and 3w per session. Total number of sessions not specified. Acupuncture = Scalp acupuncture (GV16, GV 24); sensory area (not specified); body acupuncture (ashi points, LI4, HT7, PC6, ST36, SP6, LR3; EA for ashi point (discontinuous wave 100Hz); Needle manipulation (GV16 reducing and remove needle after deqi, other points even, reinforcing, reducing)	Rehabilitation programme (massage at stumps 20min twice daily, muscle exercises 10 min once daily, kerotherapy* 30-60 min once daily, psychological involvement)	Acupuncture + rehabilitation better improved PLP than rehabilitation alone PRI A=1.12±1.36, C=6.12±5.89 ($p<0.05$); VAS A=0.17±0.80 C=1.82±1.91 ($p<0.05$); PPI A=0.19±0.32 C=1.03±1.32 ($p<0.05$)	At 3m acupuncture group still had significantly reduced PLP PRI A=1.28±1.44 C=6.84±6.29 ($p<0.05$); VAS A=0.47±1.72 C=2.05±2.09 ($p<0.05$); PPI A=0.31±0.86 C=1.33±1.33 ($p<0.05$)

Study	Country	Study type; (sample size)	Reason for amputation; time since amputation; type of amputation; participant age	Intervention	Control	Outcomes	Long term follow up
Liaw *et al.* (1994) (English)	Taiwan	NRCT; (n=57)	Mostly trauma; A=<1w-6m, C=N/A; UL(A=9, C=5) LL (A=15, C=22) Bilat (A=1, C=2); A=17-78y, mean 39.9y, A=18-76y, mean 46.1y	Acupuncture CLS (ipsilateral for bilateral amputation) for 30 mins after obtaining deqi. Treatment 1-2X daily for 1-7 treatments Study had three groups (based on time of receiving acupuncture treatment after the onset of PLP). G1=within 1w, G2=by 2w, G3=3w-6m	Usual care (medication and physiotherapy)	Acupuncture relieved PLP and reduced total period of suffering compared to usual care especially if given within 1w. VRS G1=1.45±1.52; G2=1.75±1.73; G3=3.94±2.86; C=1.81±2.22	None

Key: NRCT=non-randomised controlled trial, A=acupuncture group, C=control group, G=group, UL=upper limb, LL=lower limb, bilat=bilateral, w=week, m=month, y=year, CLS=contralateral side, VRS=verbal rating scale, PRI=pain rating index, VAS=visual analogue scale, PPI=present pain intensity. *kerotherapy or wax therapy involved applying molten paraffin wax to the residual limb

Figure 2.7 Flow diagram of further studies identified in the updated literature search on the effectiveness of acupuncture for treating phantom limb syndrome



Alongside the systematic review a narrative review of the 36 case studies identified (28 reporting on acupuncture intervention) during the systematic review was completed. As the majority of the case studies were in Chinese, this was also undertaken in collaboration with colleagues and again is therefore not reported in this thesis but the publication is included in appendix 2.5.

Despite completing the narrative analysis it was unclear what the optimal acupuncture treatment was for PLSd and a variety of different approaches were taken and outcome measures used. This identified the need for further research to develop consensus on a treatment approach.

Summary of systematic review undertaken to identify the evidence base of research on acupuncture for the treatment of PLSd

- Only two nonrandomised controlled trials were identified evaluating the effectiveness of acupuncture intervention for treating PLSd, both of which had high risk of bias and were of poor methodological quality.
- 28 case studies were identified reporting on acupuncture intervention for treating PLSd. These studies used a wide variety of treatment approaches and no standardised regime could be established. The studies generally reported positively suggesting that acupuncture may be a beneficial intervention for PLSd.

2.8 Justifying the research

Although the mechanisms of PLSd are understood, there is a lack of evidence supporting the ability to prevent it. Also, despite guidelines existing for the treatment of neuropathic pain, evidence supporting the use of pharmacological interventions to manage PLSd are scarce, often of poor quality and sometimes conflicting. Non-pharmacological interventions such as mirror therapy, GMI and stump liners are often perceived as beneficial but this literature review has identified a lack of quality research supporting their use. Currently no intervention has been found to be definitively effective, suggesting other interventions such as acupuncture should be explored. Low level evidence suggests acupuncture may be an effective intervention for PLSd, but no RCTs have been identified evaluating this. These findings highlight the need for further research to assess this. However, in keeping with the MRC framework for developing and evaluating complex interventions (Craig *et al.,* 2008b), prior to assessing effectiveness, a feasibility / pilot study should be undertaken, justifying undertaking the feasibility study reported in this thesis.

No acupuncture guidelines currently exist for the treatment of PLSd. The systematic review and narrative review identifying the evidence base of research on acupuncture for the treatment of PLSd found few studies. Across these studies acupuncture was implemented in different ways, including giving acupuncture to the contralateral limb, ipsilateral limb, ear and scalp. Different frequency and total number of treatments were provided across studies and no clear guidelines could be drawn to provide information on an appropriate acupuncture protocol for use in a feasibility study. These findings identified the need for research to be undertaken within the developmental stage of the MRC framework to design an acupuncture protocol before undertaking a feasibility study.

Few qualitative studies have explored the experience of PLSd in amputees and those which have tend not to specifically report on lower limb amputees or include only participants of a similar time post amputation, indicating that PLSd needs to be better understood. Also, whilst undertaking this literature search, no papers were identified exploring the acceptability of acupuncture for treating PLSd and quantitative studies and case studies identified during the systematic review / narrative review did not report on

the acceptability of this intervention. These findings highlighted the need for further research to be undertaken within the developmental stage of the MRC framework to both obtain preliminary data on the perceived acceptability of acupuncture and to gain deeper understanding of amputees' experience of living with PLSd before undertaking a feasibility study on this demographic group.

Summary of justification for this research project

- Current evidence on the management of PLSd is poor, identifying the need for further research to evaluate the effectiveness of interventions to resolve this syndrome.
- No robust evidence currently supports the use of acupuncture for treating PLSd, identifying the need for further research in this area.
- No standardised acupuncture regime exists for treating PLSd, identifying the need to develop an acupuncture protocol before undertaking a RCT.
- Amputees' experience of living with PLSd is poorly researched, identifying the need to further explore this prior to undertaking a RCT.

Chapter 3. Methodology

3.1 Introduction

The two previous chapters identified and justified the aim and objectives of this project. Given the project's aim to develop an acceptable acupuncture protocol for the treatment of lower limb amputees with PLSd which could be implemented in a definitive multi-centred RCT, the lack of previous research in this area and the potential complexity of the intervention, the project was situated under the MRC framework for developing and evaluating complex interventions (Craig *et al.*, 2008a).

By necessity and in keeping with the MRC framework the project involved several stages (three separate studies) to achieve its aim. As these studies involved taking different epistemological viewpoints, a pragmatic approach was taken throughout the project. Methodologically, as both qualitative and quantitative methods were deemed necessary, the project took a mixed methods research (MMR) approach (Creswell and Plano Clark, 2011).

In this chapter the objectives of the project are aligned with the MRC framework for developing complex interventions and the rationale for using this framework is discussed. Pragmatism is described and the MMR design used in this project is identified. To provide clarity, procedures used are outlined and a procedural diagram is provided. Additionally the researcher's background and epistemological and ontological position is described to ensure openness and to aid reflexivity during the qualitative stages of the research described in Chapter 5 and 6.

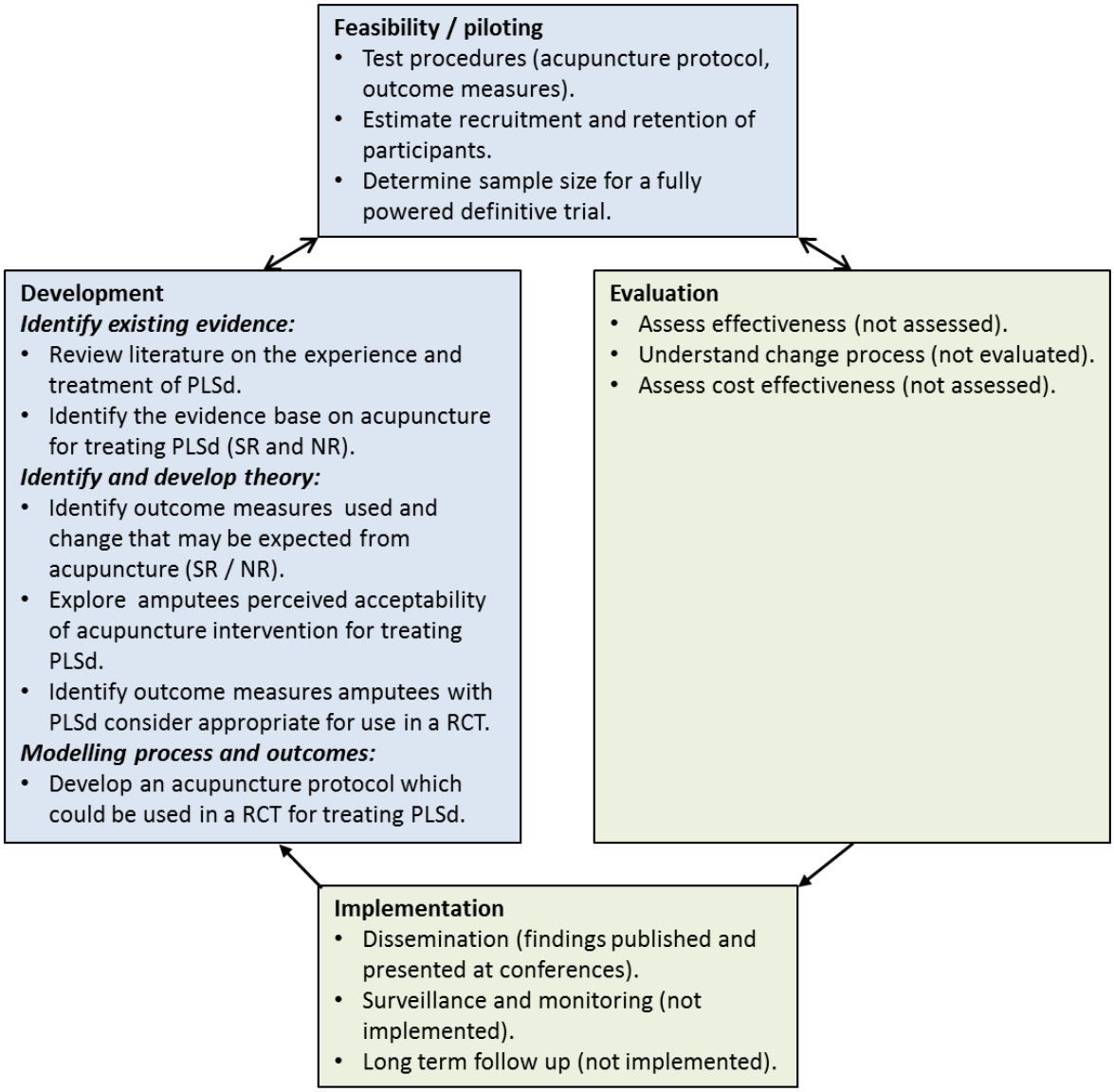
3.2 Theoretical framework of the project

No clear boundaries exist between simple and complex interventions but complex interventions usually have several interacting components and allow interventions to have a degree of flexibility (Craig *et al.*, 2008b). The intervention in this project, acupuncture, was considered complex due to its number of interacting components, such as the participant, practitioner relationship and the effect of practitioner intention when giving treatment. It was also considered complex due the degree of flexibility needed to assess practical effectiveness (how well acupuncture works in everyday practice) and the consequent pragmatic approach and flexibility needed in a research setting to stay close to everyday clinical practice.

As the project aimed to develop a complex intervention it was structured within the MRC framework for developing complex interventions (Craig *et al.*, 2008b). This framework recognises that problems often arise in evaluation due to ill-defined and ill-developed interventions and gives weight to the development and piloting / feasibility phases of research, aiming to establish effectiveness in everyday practice (Craig *et al.*, 2008a). The framework advises that interventions should be developed systematically, using available evidence and appropriate theory and that interventions should be tested using pilot / feasibility studies, before completing a definitive evaluation (Craig *et al.*, 2008b). This project aimed to undertake the developmental and feasibility and piloting steps identified under the MRC framework for developing complex interventions (figure 3.1). Evaluating effectiveness, understanding change process, assessing cost-effectiveness, surveillance and monitoring and long term follow-up were beyond the scope and funding of this PhD project. This project was undertaken as a preparatory step in preparation for a multi-centred definitive trial.

The objectives of the project were aligned with the MRC framework for developing complex interventions (table 3.1) and the structure of the project was designed in line with these recommendations; identifying existing evidence, identifying and developing theory, modelling processes and outcomes, assessing feasibility, evaluation and implementation (Craig *et al.*, 2008b).

Figure 3.1 Situating the project under the MRC framework for developing and evaluating complex interventions adapted from Craig et al. (2008a)



Key: PLSd, phantom limb syndrome; RCT, randomised controlled trial; SR, systematic review; NR, narrative review; RCT, randomised controlled trial.

Blue boxes indicate elements the study aimed to achieve .
Green boxes indicate elements which were beyond the scope of this project.

Table 3.1 Aligning the project objectives with the MRC framework for developing and assessing complex interventions

Questions researchers should ask when developing complex interventions (Craig *et al.*, 2008a)	**Project objectives**
"Does your intervention have a coherent theoretical basis?"	Ob1. Review literature on amputees' experience of PLSd. Ob2. Identify relevant research evaluating the effectiveness of interventions to prevent or manage PLSd.
"Have you used this theory systematically to develop the intervention?"	Ob2. Identify relevant research evaluating the effectiveness of interventions to prevent or manage PLSd.
"Can you describe the intervention fully, so that it can be implemented properly for the purpose of your evaluation, and replicated by others?"	Ob3. Develop an acupuncture protocol for the management of PLSd in lower limb amputees for use in a feasibility study.
"Does the existing evidence – ideally collated in a systematic review – suggest that it is likely to be effective or cost effective?"	Ob2. Identify relevant research evaluating the effectiveness of interventions to prevent or manage PLSd.
"Can it be implemented in a research setting, and is it likely to be widely implementable if the results are favourable?"	Ob4. Explore lower limb amputees' perceived acceptability of acupuncture within the context of living with PLSd, appropriateness of outcome measures and willingness to be involved in a randomised controlled trial.

Questions researchers should ask when piloting and assessing feasibility of complex interventions (Craig *et al.*, 2008a)	**Project objectives**
"Have you done enough piloting and feasibility work to be confident that the intervention can be delivered as intended? Can you make safe assumptions about the effect size and variability and rates of recruitment and retention in the main evaluation study?"	Ob5. Evaluate the feasibility and acceptability of providing acupuncture intervention to a group of lower limb amputees in preparation for a definitive multi-centred RCT evaluating the effectiveness of acupuncture for treating PLSd.

Key: Ob, objective.

3.3 Philosophical stance of the project

As the overall project was set within the framework for developing a complex intervention the research was situated under pragmatism, a paradigm which welcomes the use of mixed methods and is not troubled by issues of incommensurability (Greene 2007). Pragmatism derived from James, Peirce, Mead and Dewey and takes many forms (Creswell, 2014). It is a research philosophy which focuses on the consequence of actions, supporting combining qualitative and quantitative methods (Denzin and Lincoln, 2011) and seeking middle ground between philosophical dualisms (Robson, 2011). It offers an alternative to adhering rigidly to positivism or interpretivism (Feilzer, 2010) considering that choosing the appropriate method to answer a research question is more important than the commitment to any one paradigm and its philosophical underpinning (Robson, 2011). It places the research problem at the centre of the research (Mackenzie and Knipe, 2006) and tools from both the interpretivist and positivist paradigm can be used to collect and analyse data (Mackenzie and Knipe, 2006). Pragmatism advocates using the best methodological approach to answer a research question, whatever that may be (Robson, 2011) and draws liberally from both qualitative and quantitative philosophical assumptions (Creswell, 2014).

Pragmatism recognises the positivist and interpretivist paradigm share many commonalities with both seeking to find the truth, regardless of whether this is an objective truth or subjective truth related to multiple realities (Feilzer, 2010). Epistemologically, pragmatism views knowledge as being both based on reality and constructed (Greene, 2007). Ontologically, pragmatism takes an inclusive realism stance, where virtually everything is deemed to be real (Onwuegbuzie and Johnson, 2006) accepting that there are both singular and multiple realities which are open to empirical inquiry (Feilzer, 2010). Instead of concentrating on ontological assumptions, pragmatism draws on ‘lines of actions’, ‘warranted assertions’ and ‘workability’ (Morgan, 2007). Pragmatics believe truth is ‘what works at the time’ (Creswell, 2014).

Pragmatists believe knowledge may be obtained through a variety of methods. The research question is placed centrally with different data collection and analysis approaches applied to understand the problem (Savin-Baden and Howell Major, 2013).

In keeping with taking a pragmatic stance, in this project, methodologically the researcher rejected the incompatibility thesis stance (stating that it is inappropriate to mix qualitative and quantitative methods), and took a methodological eclecticism approach, choosing the most appropriate methodology for answering each stage of the project (Teddlie and Tashakkori, 2011).

3.4 Methodological approach of the project

As the project was complex, consisted of different research questions and clearly required a multiplistic approach to develop a protocol for a definitive trial, MMR methodology was used. Other developmental acupuncture studies also have adopted this approach (de Valois *et al.*, 2011). This was considered an appropriate approach to answer the research aim and was employed due to the project's different research objectives, which required both qualitative and quantitative approaches (Bryman, 2006), and because the project aim was developmental involving multiple studies with the results of one study informing the development of another (Greene, 2007). An MMR approach was considered acceptable as the philosophical underpinning of the project, pragmatism, embraces the mixing of methods (section 3.3).

The researcher was aware of both the philosophical and methodological issues related to MMR. There was awareness that some researchers take an incompatibility thesis stance (Creswell, 2011). The researcher understood that philosophical assumptions influenced methodological decisions such as sampling, data collection methods, analysis and quality criteria and was aware that due to integration of qualitative and quantitative methods, problems related to rigour could be exacerbated (Onwuegbuzie and Johnson, 2006). The researcher acknowledged the argument that combining both qualitative and quantitative methods can diminish the value of both (Sale *et al.*, 2002) and the limitation that there was no single recognised common vocabulary to discuss overall assessment of MMR (Onwuegbuzie and Johnson, 2006). There was understanding that MMR could lead to a complex and complicated project design (Creswell, 2011).

However, MMR was considered an appropriate methodology because it could provide more complete understanding to the research question (Creswell, 2014) and simultaneously address a wide range of questions, rather than just one or two (Teddlie and Tashakkori, 2011). The researcher took the approach that as MMR draws on qualitative and quantitative methods, it minimises the limitations of these approaches (Creswell, 2014, Creswell, 2011) and exploits the strengths of both methods (Murphy *et al.*, 2014). However, the researcher stayed mindful of the issues related to MMR and therefore considered the philosophical assumptions and justified the methodological decisions made at each stage of the research. Throughout the project, the researcher

was mindful of the differences in intent and implementation of qualitative and quantitative research. There was awareness of the difference in the role of the researcher (with qualitative approaches identifying with researcher bias whereas quantitative research considering the researcher objective and the research value free) and the different approaches to assessing quality.

3.4.1 Describing mixed methods research

MMR is a form of inquiry which combines qualitative and quantitative methods to provide depth and breadth to understanding, through either merging data or through sequentially building one upon the other (Creswell, 2011). It may involve one study or multiple studies within a program of inquiry, with each study reported separately as a distinct freestanding study (Creswell and Plano Clark, 2007). MMR can be implemented in different ways, allowing for allocation of different weighting to different methods, different interactions among the methods and different sequences of implementation (Greene, 2007). Data can be merged (bringing the data together), connected (one set of data builds another) or embedded (one set of data supports another) (Creswell and Plano Clark, 2007). The key characteristics of MMR are described in table 3.2.

Numerous different MMR study designs are reported in the literature. Greene *et al.* (1989) reviewed 57 MMR studies and identified five designs; triangulation, complementarity, development, initiation and expansion. Subsequently, many authors identified other types and it has been suggested that there are about 40 designs, of which Creswell identified the six most frequently used (Ivankova *et al.*, 2006). In this project Creswell and Plano Clark (2011) classification was used, which included six designs; convergent parallel, explanatory sequential, exploratory sequential, embedded, transformative and multiphase. This project overall took a multiphase design. With a multiphase design connected quantitative and qualitative studies are undertaken and sequentially aligned, with one study building on the next to address a central research question. Each individual study addresses a different question that addresses a larger objective. This approach can be taken to provide an overarching methodological framework to a project with multiple phases. Multiphase studies are chosen when the study objectives cannot be answered with a single mixed methods study.

Table 3.2 Characteristics of mixed methods research (MMR)

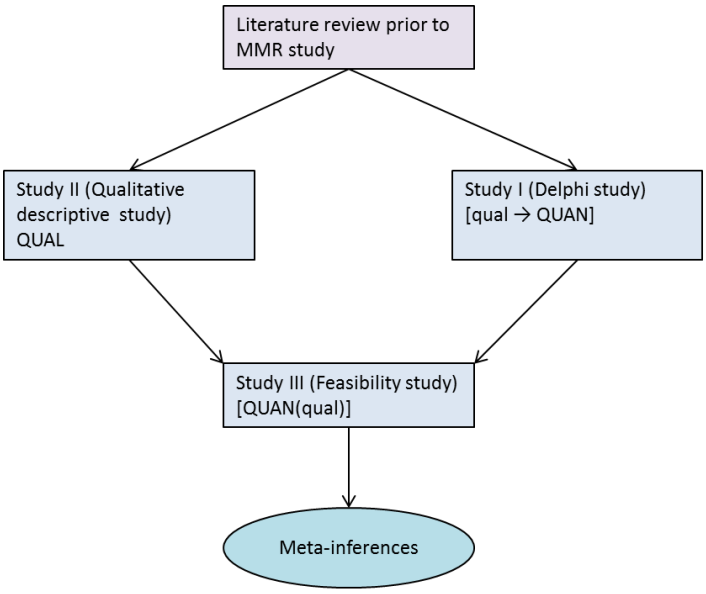
Characteristic	Description
Paradigm Pluralism:	The underlying philosophy of the research may include a variety of paradigms (Teddlie and Tashakkori, 2011). Multiple paradigms, phased-in paradigms or a single paradigm can be used in MMR, with some authors taking the stance that individual paradigms should be honoured whilst others advocate having one underlying paradigm (Creswell, 2011).
Methodological eclecticism	The best / most appropriate method is chosen to answer the research question regardless of whether it is qualitative, quantitative or mixed (Teddlie and Tashakkori, 2011).
Diversity:	MMR can address a wide range of questions and can produce divergent or dissimilar results which can then provide greater insight into a phenomenon (Teddlie and Tashakkori, 2011).
Emphasis on continua:	MMR instead of using dichotomous terms, allows for a range of options, integrated questions and innovative ways of analysing data (Teddlie and Tashakkori, 2011).
Iterative:	MMR includes both deductive and inductive logic, testing predictions, theories and hypotheses, gaining an in-depth understanding of a phenomenon and generating theory and hypotheses (Teddlie and Tashakkori, 2011). It sits somewhere along but not at one end or other of the top-down / bottom up continuum (Johnson *et al.*, 2007).
Research question	With MMR the research question is central rather than the philosophical underpinning. Research questions can be emergent (Teddlie and Tashakkori, 2011).
Set of basic research designs	There are a range of basic research designs described by different authors (Creswell, 2011). However, there is recognition that the number of design typologies can never be exhaustive (Teddlie and Tashakkori, 2011) and the view that MMR should not follow a set formula but should be an artful mix which best fulfils the intended purpose (Greene, 2007).
Balance and compromise	MMR generates data which is a balance between qualitative and quantitative. It attempts to respect both viewpoints whilst seeking a middle ground between philosophical dualisms (Johnson *et al.*, 2007).

3.4.2 Project design

As the researcher was new to MMR a typology-based approach was taken and emphasis was placed on the classification of the project design and adaptation of this design to meet the project's purpose. This approach was taken over a dynamic approach (which does not place emphasis on selecting the appropriate design) as typologies facilitate the researcher to use a pre-structured approach for addressing the research, so ensuring the research design is rigorous (Creswell and Plano Clark, 2011). This project used a multiphase design, fitting with the philosophical assumptions described earlier. The multiphase design consisted of two individual studies which were both undertaken to sequentially inform a feasibility study. One was an online Delphi study which developed an acupuncture protocol (Chapter 4), and the second was a qualitative descriptive study, which collected data through semi-structured interviews and explored the acceptability of acupuncture within the context of living with PLSd and appropriateness of outcome measures which could be used in a feasibility study (Chapter 5). Post completion of these two studies a feasibility study was conducted (Chapter 6). As can be the case with sequential designs, the feasibility study itself was MMR (Onwuegbuzie and Johnson, 2006) had an embedded design, and qualitative data were collected alongside quantitative to answer secondary research questions. In keeping with MMR a notation system was used to facilitate description of the overall project design (figure 3.2).

Overall the project was considered interactive in that the design of one study depended on the results of another (Creswell and Plano Clark, 2011). The relative importance and timing of the quantitative and qualitative phases of the project were made explicit. As shown in (figure 3.2) different levels of importance were placed on qualitative and quantitative methods at different stages of the research and overall the project timing was sequential. Overall as the project was sequential, qualitative and quantitative data were analysed separately with one study informing the design of the next (Creswell and Plano Clark, 2011). However, when considering the studies independently, the third study mixed data during results, bringing qualitative and quantitative findings together through a side-by-side comparison (Creswell and Plano Clark, 2011). Although data across studies were not formally merged, meta-inferences were drawn and the three studies informed the development of recommendations for a definitive trial.

Figure 3.2 Overview of project design: a multiphase design



Key: Uppercase letters (QUAN, QUAL) indicates priority; lowercase letters (quan, qual) indicate supplement; → sequential design; ( ) embedded design; [ ] MMR is used within a single study

3.4.3 Procedural diagram

Figure 3.3 provides diagrammatic details of the paradigm, methodology, and methods used in each stage of the project. Additionally, as procedural diagrams are recommended in MMR and can lead to better understanding of the study design, one was developed for this project (figure 3.4). Diagrams show the sequence of data collection, priority of qualitative or quantitative methods and the integration (connection and mixing point) of different data (Ivankova *et al.*, 2006). Ten rules were developed by Ivankova *et al.* (2006) for drawing visual models of MMR procedure and these were followed when designing a procedural diagram for this project.

Figure 3.3 Summary of the project's philosophical approach, methodology, and methods

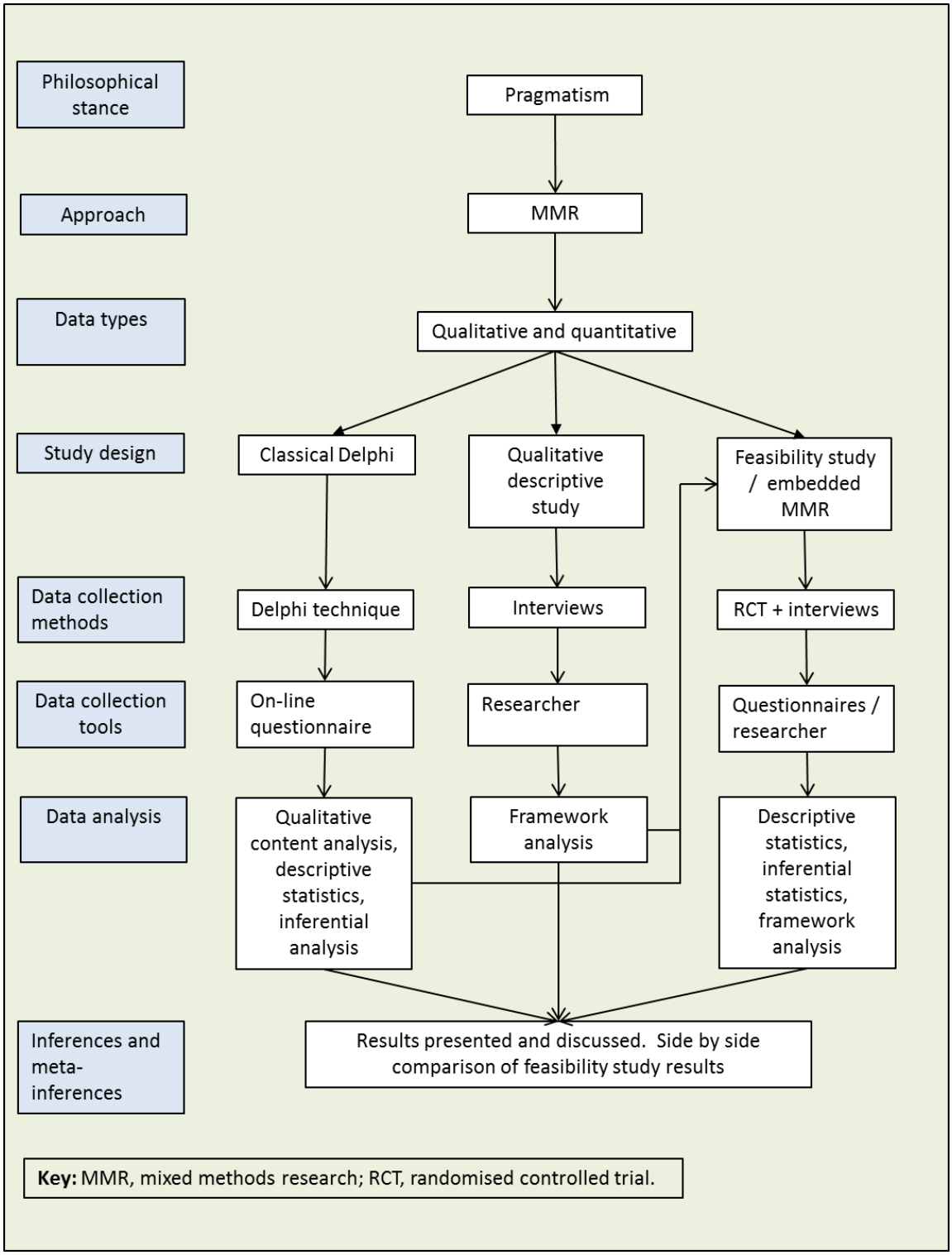
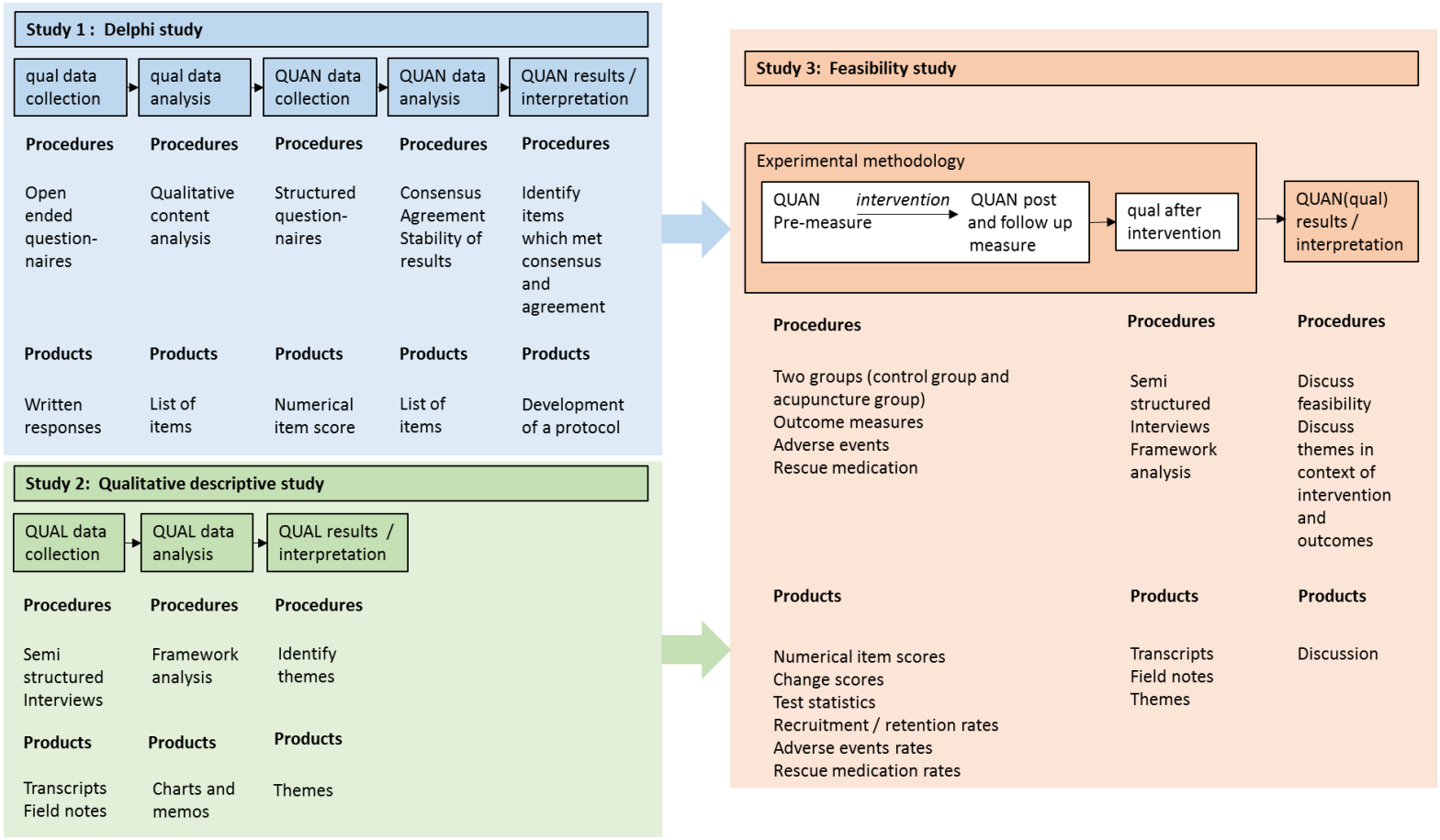


Figure 3.4 Procedural diagram of the project



Adapted from Ivankova *et al.* (2006)

3.5 Mixed methods research language used in this project

A difficulty of MMR is knowing which language to use and both a bilingual approach, combining post-positivist and constructivist terminology, and the development of new terminology have been employed (Teddlie and Tashakkori, 2011). Using a single traditional assumptive stance is generally insufficient, unless MMR is undertaken within one traditional paradigm, as quality is rooted in this philosophical framework and its assumptions (Greene, 2007). Additionally it has been argued that the combined use of qualitative and quantitative critical appraisal criteria is insufficient as MMR is more than just the sum of its qualitative and quantitative elements. Also, as MMR uses different assumptive stances and methodologies it may not be right to make judgement solely on inquiry quality using traditions of inquiry that are based on representativeness and generality; validity, reliability or contextual meaning and richness; credibility, transferability, dependability and confirmability (Greene, 2007).

Greene (2007) suggests ensuring methodological rigour through adhering both to the conventional qualitative and quantitative criteria under which the method is being implemented and through MMR specific quality appraisal when evaluating the accuracy or authenticity of conclusions. In keeping with this, in this project traditional qualitative and quantitative quality appraisal was used for each study but MMR critical appraisal frameworks were considered when appraising the overall project. Heyvaert *et al.* (2013) identified and critically appraised 13 different MMR quality appraisal frameworks. Of these nine provided separate quality criteria for the integration of methods, but of these nine only three provided detailed criteria (Dellinger and Leech, 2007, O'Cathain *et al.*, 2008, Onwuegbuzie and Johnson, 2006). Of these three, two used the same criteria of legitimation considering; sample integration, inside-outside, weakness minimisation, sequential, conversion, paradigmatic mixing, commensurability and political aspects of the integrated study. The other used traditional terms and provided a check list for good reporting of MMR. In this project as legitimation was considered the most detailed and appropriate method to assess quality and limitations, Onwuegbuzie and Johnson (2006) criteria were used.

3.6 Considering other approaches

The researcher considered MMR was the only way to answer the project aim as in the context of the MRC framework both qualitative and quantitative approaches were needed. However, a different MMR approach could have been used. A non-phantom limb pain specific acupuncture protocol could have been used in the feasibility study such as Battlefield acupuncture (Amaro, 2009). This would have avoided the need of the Delphi study, but would have meant that the protocol was not amputee / PLSd specific. Additionally Battlefield acupuncture involves auricular acupuncture which may not be considered acceptable to participants. As the researcher wanted to develop a specific protocol for PLSd, Delphi methodology was used. Amputees could have been surveyed on the perceived necessity and acceptability of acupuncture for the treatment of PLSd and on their willingness to be involved in a feasibility study. However, although this would have allowed for more generalisable findings it would have meant in depth data could not have been collected, so limiting the understanding of this syndrome. The feasibility study could have been run as a preference trial, but this would have meant that data could not be collected on acceptability of randomisation, procedures could not be fully piloted and data on effect size for use in future sample size calculations could not be generated (parametric or non-parametric tests are needed to calculate effect size and these tests make the assumption that the sample is random (Field, 2013, Pallant, 2013)). Including an embedded qualitative element to either a feasibility or preference trial was considered essential to explore participants' experience and acceptability of receiving acupuncture intervention and was in line with the MRC framework for developing and evaluating complex interventions.

3.7 Researcher's background and epistemological / ontological position

There is the view that the researcher's underlying philosophical beliefs influence inquiry, regardless of whether this is intentional or not (Greene, 2007). Therefore, to aid openness and to ensure that assumptions were explicit, the researcher's epistemological and ontological stance and background were described. Also, qualitative research (employed in the qualitative descriptive study and the feasibility study) demands that pre-conceptions are made explicit to aid reflexivity and to acknowledge the researcher's influence on research (Savin–Baden and Howell Major, 2013).

The researcher was a 39 year old, white, British female with experience of both the western and Traditional Chinese understanding of health and illness. Originally the researcher trained as a chartered physiotherapist (BSc physiotherapy) and had extensive clinical experience working within the NHS as a musculoskeletal physiotherapist. Subsequent training in TCM and 5 Element style acupuncture (MSc Acupuncture), provided an insight into treating patients under these alternative health philosophies and understanding of TCM was consolidated through spending five months in China at a TCM hospital. This dual understanding of both western and TCM / 5 element health systems, alongside the experience of working in the NHS meant that the researcher had the appropriate knowledge and background required for this project. However, with a positive attitude towards CAM in general and specifically acupuncture, this meant that there may have been a bias in favour of acupuncture.

Epistemologically the researcher subscribed neither fully to the positivist / post-positivist or interpretive paradigm and took an empathically neutral position, advocating that assumptions are made transparent as research cannot be value free (Snape and Spencer, 2003). The researcher held a coherence theory of truth view, believing that reality is gauged consensually (Snape and Spencer, 2003) and recognised that throughout the project, both during data collection and analysis, the social world may have had an impact on the research. There was acknowledgment that the researcher had a role in shaping participants' responses and recognised that gender, social status, age and other characteristics all inevitably shaped the kind of research generated (Green and Thorogood, 2009).

Ontologically the researcher adhered closely to subtle realism. The researcher rejected both relativism and realism and instead acknowledged both the influence of humans and the effect of real structure on action (Houston, 2001). The researcher believed that the world existed independent of one's knowledge of it, but also that reality is socially constructed, but not entirely so (Snape and Spencer, 2003). Different interpretations and different viewpoints may have yielded different understandings but fundamentally the researcher believed there was an external reality.

3.8 Summary

As the intervention (acupuncture) evaluated in this project was considered complex and as the project sought to develop a feasible protocol for use in a definitive trial, the project was situated under the MRC framework for developing complex interventions. The project's objectives were aligned using this theoretical framework. Time was therefore spent developing an acupuncture intervention, exploring amputees' perceived acceptability of acupuncture within the context of living with PLSd and evaluating the feasibility of completing a RCT. These developmental / feasibility stages are discussed in the following chapters of this thesis.

Philosophically a pragmatic approach was taken during the project as this was felt most in keeping with its theoretical design. The overall project methodologically was multiphase MMR, and within this design were three separate sequential studies. Two of these studies both informed the development of the third, a feasibility study. These three studies are described in Chapters 4-6. When reflecting on methodological rigour, terminology was used appropriate to the qualitative or quantitative methods employed. Integration of the studies and overall methodological quality are discussed in Chapter 7.

Summary of project methodology

- The project was situated under the MRC framework for developing complex interventions.
- A pragmatic philosophical approach was taken throughout the project.
- Methodologically the project used a multiphase MMR design consisting of three separate sequential studies.

Chapter 4. Developing an acupuncture protocol for treating lower limb amputees with phantom limb pain

4.1 Introduction

The literature review chapter (section 2.7) identified that a variety of different styles, regimes and approaches were adopted when treating PLSd with acupuncture and that there was the need for further research to develop consensus on a treatment approach before designing a RCT. This chapter describes the development of an acupuncture protocol for the treatment of PLSd. In keeping with the theoretical framework of this project, time was spent systematically developing this protocol. The protocol was then tested in a feasibility study (Chapter 6).

This chapter discusses the use of Delphi methodology to obtain practitioner consensus on the general principles of treatment of PLSd to develop an acupuncture protocol for its management in lower limb amputees. In keeping with the project design (multiphase design taking a sequential approach) this study was a separate study in its own right, but results of this study informed the development of the feasibility study (discussed in Chapter 6). The specific methods used in this study, results obtained and a discussion of results is presented. In the methodology section the term expert, Likert scales and methods of qualitative and quantitative data analysis used within the Delphi process are considered. The specific methods used are described and results present a finalised protocol which could be used by acupuncture practitioners when treating PLSd both in research and clinical practice. The final section debates findings from the study and implications for designing a RCT. The publication of this study is included in appendix 4.1.

4.2 Objectives

This chapter addressed the project objective described in the introduction (figure 1.1):

- Develop an acupuncture protocol for the management of PLSd in lower limb amputees for use in a feasibility study.

As described in the introduction (figure 1.2) the component parts of this objective were to obtain consensus on:

- TCM pathology and principles for treating PLSd.
- Style of acupuncture (auricular / body / scalp) used to treat PLSd.
- Treating the contralateral and / or ipsilateral limb.
- Acupuncture point choice for treating PLSd.
- Use of adjunctive treatments.
- Recommended frequency of treatment.
- Recommended total number of treatments.
- An acupuncture protocol for the treatment of PLSd.

4.3 Delphi methodology

Three main approaches of formal consensus have been used in the health field; Delphi method, nominal group technique, and consensus development conference (Murphy *et al.*, 1998). Both nominal group technique and consensus development conference require face to face contact (Murphy *et al.*, 1998) which risks introducing bias due to geographical location of participants (Becker and Roberts, 2009). Delphi technique has the advantage of not requiring face to face contact, so facilitating a wider group of participants and avoiding location bias, whilst still having the ability to guide group opinion towards a final decision (McKenna, 1994). The Delphi method allows for a greater number of individuals to be involved than would be able to interact face to face (Green *et al.*, 1999). For these reasons, Delphi was the chosen consensus methodology for this study. A review paper, by the author, on Delphi methodology is included in appendix 4.2.

Delphi consensus technique evolved due to limitations of traditional methods used to gain group opinion for policy development (Goodman, 1987) and was founded on the premise that unstructured, face to face group predictions were weaker than individual statistical predictions (Keeney *et al.*, 2011). The original Delphi method was developed in the 1950s by Olaf Helmer, Norman Dalkey and Nicholas Rescher of the Rand Corporation (Keeney *et al.*, 2011) and it has subsequently been used in healthcare, marketing, education, information systems, transportation and engineering (Rowe and Wright, 1999). The purpose of Delphi is to achieve consensus of opinion where none previously existed (Keeney *et al.*, 2011). Delphi technique involves the systematic collection and aggregation of informed judgements from a group of experts on specific questions and issues. It has been defined as a method of obtaining reliable consensus of opinion from a group of experts through a series of questionnaires interspersed with controlled feedback (Rowe and Wright, 1999) and provides information on group opinion only (Powell, 2003).

Delphi technique is appropriate in situations where there is a lack of agreement or incomplete knowledge and can provide consensus where there is uncertainty or lack of evidence (Powell, 2003). It is intended for use in forecasting and judgement situations where statistical methods are not practical or possible and it is not intended to challenge

statistical or model based procedures (Rowe and Wright, 1999).

Delphi technique involves four main characteristics; anonymity between participants, iteration with controlled feedback of group opinion, statistical aggregation of group response and expert input (Goodman, 1987). Anonymity allows participants to express and change views privately (Rowe and Wright, 1999), iteration with controlled feedback allows participants to 'communicate' with each other, informing participants of others' perspectives (Powell, 2003) and allowing participants to change their views (Skulmoski *et al.*, 2007) and statistical aggregation of group responses allows for data to be quantitatively analysed and interpreted (Skulmoski *et al.*, 2007). Strengths and weaknesses of the Delphi technique in relation to these characteristics are documented in table 4.1.

4.3.1 Delphi techniques

The original / Classical Delphi technique involved an unstructured first round seeking open responses, which were analysed using qualitative methods. Subsequent rounds sought quantification of the first round through ranking techniques. Feedback of group results to participants was provided, encouraging convergence to a consensus of opinion (Powell, 2003). Sample size was not determined by statistical processes but based on the qualities of the panel rather than its size (Powell, 2003). Participants were a homogenous group of experts (Goodman, 1987). The process of data collection stopped when consensus was reached, theoretical saturation achieved or when sufficient information had been exchanged (Skulmoski *et al.*, 2007) and originally involved four rounds (Keeney *et al.*, 2001).

Subsequent modifications of the Classical Delphi technique arose. Some authors advised that participants should be drawn from varied backgrounds to ensure a wide base of knowledge, whilst others maintained that studies concerned with a clinical intervention should include only specialists in that field (Powell, 2003). Modifications identified by (Keeney *et al.*, 2011) are listed in table 4.2 but making modifications has been criticised as posing a threat to the reliability and validity of results (Keeney *et al.*, 2001).

Table 4.1 Strengths and weaknesses of Delphi studies

	Strengths	Weaknesses
Anonymity between participants	Encourages truthful opinion which is not influenced by peer pressure or other extrinsic factors (Keeney et al., 2011). Avoids domination by powerful individuals and releases participants from group inhibition (Powell, 2003).	May encourage a lack of accountability (Goodman, 1987). May lead to results that are hasty and ill considered (Goodman, 1987).
Iteration with controlled feedback of group opinion	Allows participants to refine views in light of group opinion without 'losing face' (Rowe and Wright, 1999). Controlled feedback comprises of opinions from all group members rather than just the most dominant (Rowe and Wright, 1999).	Feedback may persuade participants to change their views to conform to others, rather than provide true ratings of agreement (Goodman, 1987). Attaining consensus may reflect a normative rather than an informational influence (Powell, 2003). Participants do not have an opportunity to discuss issues or elaborate their views (Keeney et al., 2001).
Statistical aggregation of group response	Allows for quantitative interpretation of the data (Skulmoski et al., 2007). Each opinion is given equal weighting of importance during analysis (Keeney et al., 2001).	Consensus may mask a bimodal or flat response distribution (Goodman, 1987) and therefore data on dispersion of scores should be provided (Powell, 2003).
Expert input	Collects data from informed individuals (Keeney *et al.*, 2011).	Experts may not exist (Goodman, 1987). Defining participants as experts is contentious and potentially misleading (Keeney et al., 2001). Including a criterion for experts risks introducing bias (Keeney et al., 2001).

Table 4.2 Characteristics of different Delphi techniques adapted from Keeney et al. (2011)

Delphi technique	Characteristics
Classical Delphi	Open first round to generate ideas and opinion. Uses three or more rounds.
Modified Delphi	The first round is modified and may consist of interviews or focus groups. May use less than three rounds.
Decision Delphi	As classical Delphi but focuses on making decisions not consensus.
Policy Delphi	Agrees future policy.
Real time Delphi (consensus conference)	Participants may be in the same room and consensus is reached in real time.
e-Delphi / Online Delphi	As classical Delphi but administered online.
Technological Delphi	As real time Delphi but uses technology to allow participants to respond. Provides instant feedback allowing participants to immediately move on to the next round.
Argument Delphi	A derivation of policy Delphi focusing on the production of relevant factual arguments.
Disaggregative Delphi	Conducts various scenarios for discussion and does not aim to meet consensus. Uses cluster analysis.

4.3.2 Using Delphi technique to develop a protocol in complementary and alternative medicine

Delphi technique has often been used in CAM to establish good practice, develop guidelines or establish key components of an intervention. Lai *et al.* (2015) established characteristics of good practice when using Chinese herbs to treat polycystic ovary syndrome and generated 85 guideline statements. Ward *et al.* (2014) used a three round Delphi process to establish key components of a yoga intervention for musculoskeletal conditions and developed a 33 item list. Smith *et al.* (2012a) used Delphi technique to develop an acupuncture protocol for women undergoing assisted reproductive technology and developed seven treatment parameters. The researcher,

as an acupuncture practitioner considered it possible and appropriate to use Delphi technique to develop an acupuncture protocol for treating PLSd.

The researcher recognised that within TCM, diagnosis and treatment of PLSd is individualised and that a fixed and rigid protocol would not be appropriate or possible. However, the researcher believed that it was possible and in keeping with TCM to develop a flexible protocol which still required practitioners to diagnose and treat patients individually, but could be used to give guidance, and be used in a RCT. TCM textbooks provide details on differential diagnosis of pathologies such as low back pain and provide suggestions on acupuncture point choice and treatment techniques (Xinnong, 1999, Maciocia, 1994 and Flaws and Sionneau 2005). This study aimed to develop guidelines, similar to those provided in textbooks, to give practitioners suggestions on the differential diagnosis of PLSd and recommend possible points and treatment techniques when treating this pathology.

4.4 Study specific methodological considerations

4.4.1 Expert panel

In Delphi studies participants are often referred to as experts, defined as 'informed individuals', 'specialists', and those with knowledge about a specific subject (Keeney *et al.*, 2001). Experts are required to have; experience and knowledge of the issue being investigated, willingness and capacity to participate, time to participate and adequate communication skills (Skulmoski *et al.*, 2007). However, within this criteria, there is debate as to how to define knowledge and experience. Knowledge may be recognised through a professional qualification or registration, but this alone does not equal expertise. Equally, experience, such as number of years in practice does not necessarily equal expertise (Baker *et al.*, 2006). Many authors recognise the difficulty of setting an inclusion criterion which ensures labelling participants as experts is not misleading (Keeney *et al.*, 2001). However, conversely, setting too narrow a definition can reduce sample size availability (Baker *et al.*, 2006). In this study participants were not described as 'experts' (section 4.5.1).

4.4.2 Qualitative data analysis

Little guidance exists on how to manage first round qualitative data (Green *et al.*, 1999) but content analysis is frequently recommended (Hasson *et al.*, 2000, Powell, 2003). Content analysis describes analytical approaches ranging from impressionistic and intuitive to systematic and strict textual analysis (Hsieh and Shannon, 2005) and two main approaches exist; quantitative and qualitative (Graneheim and Lundman, 2004).

Qualitative content analysis (QCA) explores textual data with a view to grouping together similar passages and identifying key issues (Burnard, 1996). It involves coding according to a classification scheme (Kondracki *et al.*, 2002), provides a systematic and objective method and is concerned with meanings, intentions, consequences and context (Cavanagh, 1997). Three approaches of QCA were identified by Hsieh and Shannon (2005); conventional content analysis, directed content analysis and summative content analysis (figure 4.1). In this study a directed approach was used (section 4.5.4).

Figure 4.1 Characteristics of conventional, directed and summative content analysis

- Conventional content analysis is generally used when the aim of the study is to describe a phenomenon. Researchers avoid using preconceived categories and instead allow categories to inductively develop from the data. Information is gained without imposing preconceived categories or theoretical perspectives.
- Summative content analysis quantifies certain words or content and attempts to understand the latent context and explore usage of these words .
- Directed content analysis validates or extends a theoretical framework or theory. Prior to reading transcripts, key concepts or variables are identified as initial coding categories. On reading the transcript all text that is related to an *a priori* category is highlighted and coded using the predetermined categories where possible. Any text that cannot be categorised using the initial coding scheme is analysed to determine if it represents a new category or subcategory.

(Hsieh and Shannon, 2005)

4.4.3 Consensus

An important issue in Delphi studies is defining what is meant by consensus. The definition may depend on the question being asked and may vary on the implication of the research (Keeney *et al.*, 2006). Consensus has been described both as a means of seeing whether agreement exists (Becker and Roberts, 2009) and as a stopping guideline (Holey *et al.*, 2007).

No agreement exists in the literature on the best criteria to determine consensus (Holey *et al.*, 2007) and consensus has been conceptualised differently across Delphi studies. Consensus may be determined through the aggregate of judgment, subjective level of central tendency or by confirming stability (Holey *et al.*, 2007) and can be determined within rounds or between rounds (Becker and Roberts, 2009, Holey *et al.*, 2007). Consensus within rounds typically measures the agreement of the individual participant with the statement, which then provides group opinion and the extent to which participants agree with each other. Consensus between rounds measures stability of response and can indicate whether consensus was present throughout, whether it developed between rounds and whether it changed between rounds (Becker and Roberts, 2009).

Empirically consensus was determined through measurement of variance in response, with a reduction in variance being taken to indicate greater consensus (Rowe and

Wright, 1999). However, stability of response has been argued to be the more reliable indicator of consensus (Crisp *et al.*, 1997). There is however also the opinion that stability of response measures reliability of results not consensus (Murphy *et al.*, 1998) and that the terms reliability, agreement and consensus are different with each measuring different things. Reliability measures the proportional consistency of variance among raters (Murphy *et al.*, 1998), agreement measures the extent to which participants agree with the statement under consideration and consensus measures the extent to which participants agree with each other (Keeney *et al.*, 2006). Therefore measures of reliability (stability of response) should not be used as a measure of consensus (Murphy *et al.*, 1998).

Previous studies have used a variety of methods to define consensus. A systematic review including 80 Delphi studies identified five main methods used to achieve consensus. These included; (1) median scores above a pre-defined threshold and a high level of agreement between panel members, for example, median score above a certain level and a certain percent of overall rating being in the lowest or highest tertile, (2) median score greater than a predefined threshold, (3) proportion of experts rating the indicator within the highest region of the scale was greater than a pre-defined threshold, (4) Rand criteria, (5) interpercentile range or interpercentile range adjusted for symmetry (Boulkedid *et al.*, 2011). Another systematic review of a random sample of 100 Delphi papers found that of the 72 which defined consensus, 25 used percent agreement, 16 proportion within a range, 8 measures of central tendency (such as median), 7 measures of central tendency within a specific range, 6 variance such as interquartile range (IQR), 4 formal measures of agreement such as intraclass correlation coefficient, 4 Rand criteria, 1 stability and 1 rank (Diamond *et al.*, 2014).

Williams and Webb (1994) advises that *a priori* a numerical level of consensus should be set and (Holey *et al.*, 2007) advise doing this may reduce research bias. However, in the systematic review by Diamond *et al.* (2014) only 43 of the included 100 studies provided an *a priori* specific threshold for consensus.

In this study consensus was used as a means of seeing if agreement existed and was set *a priori.* Agreement, reliability and consensus were viewed as different with consensus being defined using IQR (section 4.5.4).

4.4.4 Stability of response

Stability of response measures reliability of results and refers to the level of agreement between rounds. The Chi-squared has been used to test for stability, but there has been advice against using it in Delphi studies as it determines "the independence of the rounds from responses found in them" and not the stability of response between rounds (Holey *et al.*, 2007). Kappa statistics have been advocated with high or increasing kappa values demonstrating stability of individual's views within the group (Holey *et al.*, 2007). However, Kappa is a measure for nominal scale agreement and assumes that rating has no natural ordering (von der Gracht, 2012). Tests which are suitable for use on ordinal data to test stability of response in Delphi studies include the Wilcoxon matched-pairs signed rank test, which works with paired data of the same group of individuals in a before and after situation. Responses are considered stable when there is no significant change (von der Gracht, 2012). Stability of response has also been reported in some Delphi studies by providing data on the median and IQR across rounds (Becker and Roberts, 2009, Ward *et al.*, 2014). In this study stability of response was measured using the Wilcoxon matched pairs signed rank test and data were provided on the median and IQR across rounds (section 4.5.4).

4.4.5 Likert scale

Delphi literature does not provide clear recommendation on the optimal number of response categories for Likert scales. Many use a five point scale (Becker and Roberts, 2009, Smith *et al.*, 2012b) but others have used four point, (Smith *et al.*, 2012a) six point, (Kojima *et al.*, 2013) and eleven point (Fernandes *et al.*, 2013) scales.

The reliability and validity of a scale is affected by the number of response alternatives with two, three and four point scales providing poor validity and discriminating power (Preston and Colman, 2000). Increased number of response categories improves factorial validity (Lozano *et al.*, 2008) but increased responses may also lead to inconsistency in category interpretation, leading to misleading results, with categories with homogeneous responses being arbitrarily divided (Jones and Loe, 2013). Test-retest reliability has been reported to decrease for scales with more than 10 categories (Preston and Colman, 2000). Lozano *et al.* (2008) advises an optimal number of

categories between four and seven with less than four being associated with poor validity and more than seven only causing marginal improvements. Preston and Colman (2000) assessed participant preference and found that two, three and four response categories were least preferred and scales of seven, nine and ten most preferred.

Likert scales can either provide a midpoint (odd number of categories) or not (even number of categories). Including a midpoint allows participants to remain neutral but may also be interpreted as "don't know", "undecided" and "no opinion" (Raaijmakers *et al.*, 2000). The inclusion of a midpoint category has been suggested to affect reliability and validity as midpoints may be used as a "dumping ground" (Tsang, 2012). In this study a six point scale was used (section 4.5.3).

Summary of Delphi methodology

- Delphi technique was considered the most appropriate consensus methodology for use in this phase of the study as it did not require face to face contact.
- Delphi technique does have limitations; many different ways are used to conceptualise consensus and the words consensus, stability and agreement are often used interchangeably.
- No consensus is available on the best size of Likert scale to use in a Delphi study.

4.5 Methods

To avoid taking a disparate approach which could reduce methodological rigour (Green *et al.*, 1999) a Classical Delphi approach was taken but administered online (Online Delphi). An electronic medium was used as it provided advantages to both the researcher and participant, eliminating the task of transcription and allowing quick turnaround times (Skulmoski *et al.*, 2007). The study was quasi anonymous (the researcher knew which response came from each participant but participants did not).

As a broad understanding of views was sought, and as expert and non-expert opinion may make little difference to outcomes (Baker *et al.*, 2006) both participants with and without past experience of treating PLSd were included in the study. Two parallel Delphi studies were completed; one involving participants with past experience of treating PLSd (TPLSd) and the other involving participants with no past experience of treating PLSd (NTPLSd).

4.5.1 Recruitment, sample size and inclusion criteria

Participants were recruited by email. The British Acupuncture Council, the Association of Traditional Chinese Medicine and the Acupuncture Association of Chartered Physiotherapists were emailed with details about the study and requested to forward details on to their members. The Acupuncture Association of Chartered Physiotherapists was included as many physiotherapists practice acupuncture and have a wide breath of experience in treating musculoskeletal and pain conditions. In addition, universities teaching acupuncture were also contacted and requested to forward details of the study to past students and practitioners recommended during the recruitment process were also emailed. Any participants who contacted the researcher about the study were e-mailed a participant information sheet (appendix 4.3) and participants were requested to email back to confirm participation, which as explained on the information sheet, was taken as consent to participate. Those who agreed to participate were sent via e-mail a link to the survey website.

In keeping with the classical Delphi approach non-probability sampling was used. As it was anticipated that few practitioners would have had experience in treating PLSd with

acupuncture, convenience sampling and snowball sampling were used. This sampling methodology was chosen as the study aimed to include as many participants as possible with past experience of treating PLSd. No set panel size is recommended in the literature for Delphi studies and panel sizes ranging from 4 to 3000 have been used in health applications (Cantrill *et al.*, 1996). For a homogenous sample, a small sample size is appropriate such as 10-15 participants (Skulmoski *et al.*, 2007) or 8-12 participants (Keeney *et al.*, 2011) and this study aimed to recruit approximately this number of participants to each group.

To meet the inclusion criteria participants were required to; (1) have completed a recognised training in acupuncture, (2) be registered with a professional body, (3) have at least 3 years' clinical experience in practicing acupuncture, (4) have capacity and time to participate, (5) have the ability to communicate in English. Due to the difficulties in defining experts (section 4.4.1) this title was not used in this study regardless of participants' past experience and the inclusion criteria was not used to define an 'expert panel'.

4.5.2 Iteration

Although classical Delphi used four rounds, this has been modified by many researchers to fewer rounds (Keeney *et al.*, 2011). Two or three rounds are preferred (Hasson *et al.*, 2000) as increasing number of rounds increases participant fatigue and a fall in response rate (Skulmoski *et al.*, 2007). In this study, regardless of level of consensus achieved, to avoid participant fatigue and to minimise attrition, it was agreed *a priori* that the study would include three rounds only. A fourth round which did not involve ranking individual statements was also included which involved rating and commenting on the finalised protocol.

Participants were asked to respond to each round of the questionnaire within 7-10 days (as recommended by Keeney *et al.* (2011)) and each round closed after two weeks. To maintain participant interest and minimise attrition subsequent rounds were sent out two weeks post closure of the previous round. The use of reminders is endorsed in general texts for surveys (Edwards *et al.*, 2002). To ensure participants stayed committed, between rounds emails were sent thanking all panel members who had

returned the questionnaire and reminding those who had not yet done so to do it.

4.5.3 Questionnaire

All questionnaires were developed using Bristol Online Survey (http://www.survey.bris.ac.uk). Round one questionnaire was piloted prior to use in the study and due to feedback, to reduce participant fatigue, some questions were excluded, modified or converted from open questions to multiple choice. All participants were given an ID number to allow the researcher to link responses, follow up non-responses and remove names from questionnaires.

In round one, two hypothetical case studies were presented to participants with a range of open ended and multiple choice questions about each case (figure 4.2 / appendix 4.4). The questionnaire comprised of 12 questions per case study and were the same for each case study. This approach was chosen as it was representative of clinical practice, analysing information obtained from patients, forming a TCM diagnosis of patient pathology and deciding on an appropriate treatment plan.

Figure 4.2 Case studies presented to participants in the Delphi study

- **Case study 1:**

  A 75 year old male with a 20 year history of type II diabetes had been suffering long term diabetic neuropathy and peripheral arterial disease (atherosclerosis). He developed an ulcer in his left toe due to the neuropathy and peripheral arterial disease which eventually led to him having a left transtibial amputation (amputation through the lower limb but maintaining the knee joint) 15 days ago. Prior to surgery he suffered from numbness and pain for over a year in both lower limbs and especially the soles of the feet due to the diabetic neuropathy (sharp stabbing, shooting sensations and a loss of sensation) and his ankles and feet were swollen and cold to touch. Symptoms were aggravated by cold weather and eased with warmth.
  Post amputation the patient complained of phantom limb pain and stump pain in his left lower limb. Pain was described as heaviness in the stump and a feeling that the missing limb was constantly twisted and contracted. Constant pins and needles and intermittent sharp electric shock like sensations were felt in the missing limb especially the foot. Phantom limb pain was rated 8/10 in intensity and was constantly present.
  History of present disease: Type 2 diabetes, poorly controlled blood sugar (sometimes high / sometimes low), loose stools, normal appetite, normal sleep and regular urination, dark pale tongue with white coating, deep thready pulse.

- **Case study 2:**

  A healthy 40 year old male had been involved in a road traffic accident 2 weeks ago which resulted in a right hip disarticulation, (amputation through the hip joint, removing the entire leg). Prior to amputation the patient was in good general health. He had suffered occasional low back pain (due to prolonged sitting at a desk at work) but was otherwise well.
  Post amputation the patient complained of constant stabbing and shooting pain in his missing limb (7/10 intensity) especially deep in the thigh where it was injured in the road traffic accident. The patient also complained of poor sleep, stress and emotional upset, poor appetite and slight constipation. Tongue was purple / dark with a red tip and pulse was choppy

In round two, statements generated from analysis of round one were presented as items and participants were asked to rate each item on a 6 point Likert type scale from 'strongly agree' to 'strongly disagree'. Items were grouped into responses to each of the 12 questions from each case study in round one to allow participants to see statements within the context of the original question.

Round 3 questionnaire was as round 2 but also provided additional information, giving the individual's response from the last round and the overall group response. Both central tendency (median) and a measure of dispersion (quartiles) were provided. It was assumed that participants had not had training in the interpretation of statistics so data were presented simply using the terminology average and spread of results, defined as the middle 2 quarters of the range of values, to ensure the information was basic but meaningful.

To minimise participant fatigue, questions in which 50% or more of the ranked statements had met consensus in round two were not included in round three unless agreement had not been met (agreement = median score of 5-6). However, within questions included in round three, ranked statements which had met consensus were not omitted to avoid introducing bias (table 4.3). By excluding statements which have met consensus, statements which have not met consensus have the potential to rate higher levels of consensus and possibly higher ratings of importance in the final score than statements which reached consensus and were omitted earlier in the questionnaire (Keeney *et al.*, 2011). A summary sheet of statements which had met consensus was provided with round 3.

In the final round, a proposed protocol was presented to participants. Participants were asked to comment and rate their overall level of agreement of the protocol on a six point Likert scale.

Table 4.3 Example of question and statements included and excluded from round three

What would be your main treatment principles when treating this patient?

Statement	Median	Quartiles	IQR (Q3-Q1)	Range	No comment
Reduce pain	6	6-6	0	0	0
Move qi and blood	5	5-6	1	2	0
Drain damp and transform phlegm	4.5	4-5	1	1	1
Tonify spleen qi	4	4-5	1	3	0
Tonify and warm kidney yang	6	4-6	2	2	2
Eliminate cold and warm the channels	5	4-6	2	2	0
Regulate liver qi	4	2.75-5	2.25	3	1

Key:

Agreement met (median score ≥ 5-6).

Agreement not met (median < 5).

Statements above this line had met consensus. Statements below this line had not met consensus (consensus defined as IQR ≤ 1.75).

A six point Likert scale was used during all phases of the study. This size scale was chosen as it was large enough to be valid and reliable and small enough to minimise the risk of the same meaning being arbitrarily divided due to inconsistency in interpretation. An even scale was chosen to avoid misinterpretation of midpoint and to encourage participants to make active positive or negative decisions about items (section 4.4.5). The scale ranked from 1 (strongly disagree) to 6 (strongly agree). A separate category of "no comment" was provided due to the varied nature of participants' acupuncture training. It was recognised that variations in training may mean that the terminology of

some items may have little meaning to some participants. Where this was the case participants were advised to tick "no comment".

4.5.4 Data Analysis

Qualitative data were analysed using the software NVIVO 10 and quantitative data were analysed using SPSS version 21. In round one, QCA, taking a directed approach was used. Questionnaires were read through several times and data were divided into units of coding using thematic criteria. Each unit of coding was grouped under a predetermined category / subcategory and if no category fitted a new category was developed. Data in each coding unit were condensed to delete anything superfluous, whilst still preserving the core using progressive summarisation (figure 4.3). Finally subcategories were cut down where possible by aggregating with others and data in each category were ranked in order of frequency of codes.

Figure 4.3 Example of progressive summarisation

Qu 2. (CS 1 TPLSd) What would be your main treatment principle when treating this patient?

Unit of coding (Participant Quote)	Progressive summarising	Condensed statement for round 2 Delphi
"Move Qi and circulation"	move qi and circulation	move qi and blood
"Regulate Blood and Qi in lower limbs"	move qi and blood in lower limbs	
"Disperse qi stagnation and invigorate Blood"	move qi and blood	
"Break Blood stagnation"	clear blood stagnation	
"Move Qi and blood"	Move Qi and blood	

Analysis focused predominantly on the manifest context of the data. Due to the large volume of data created in round one, to make round two manageable, a reductionist approach was taken and a threshold was applied for inclusion in round two. Condensed statements which only appeared once were excluded from round two.

A consistency check of coding was applied by testing intra-rater reliability 10-14 days post initial coding. Inter-rater reliability was checked through a second coder coding a portion of the data. The researchers discussed doubts and problems with the definitions of categories, coding rules and categorisation of data and issues were resolved. Categorised and condensed statements were discussed and reviewed to ensure meaning was not lost or biased through researcher interpretation. The QCA rules applied in this study were as recommended by Schreier (2012) and are provided in figure 4.4.

Figure 4.4 Qualitative content analysis rules applied in the Delphi study

QCA Rules Applied in this study:

- Main categories were uni-dimensional.
- Subcategories were mutually exclusive. The same unit of coding was only assigned to one subcategory.
- The coding frame was exhaustive.
- A miscellaneous category was included to capture unexpected / infrequently reported data.
- Each category was defined so that the researcher and others consistently knew what the category meant. Categories were defined by:
    - Name.
    - Description of the name (describe features of the category).
    - Examples (positive or negative to describe what the category was / was not).
    - Rules (if subcategories overlapped to define which one to use).
- The coding frame was revised during the coding phase.
- The coding frame was not changed during categorisation of data.

Quantitatively, to ensure participants have some indication of the extent of consensus, it is recommended that aggregation should include both central tendency and an indication of dispersion (Murphy *et al.*, 1998). In the synthesis of consensus data median is considered more robust to the effect of outliers than mean (Murphy *et al.*, 1998). As data produced in round 2 and subsequent rounds were ordinal and to reduce the effect of outliers, aggregation of data for feedback to participants used median and quartile values (Svensson, 2001).

The purpose of consensus in this study was to see if agreement existed and consensus was not used as a stopping guideline. To reduce research bias *a priori* criteria for defining consensus and agreement were set. Median and IQR values were used. As

stability of response measures reliability of results, not consensus, it was not used as a measure of consensus. IQR value depends on the number of response choices (Rayens and Hahn, 2000). An IQR of ≤ 2 is considered an appropriate measure of consensus on a 10-unit scale and an IQR of ≤ 1 on a 4-5 unit scale (von der Gracht, 2012). Taking into consideration the size of the Likert scale in this study and the demands lengthy further rounds (through statements not reaching consensus) put on participants, a group median of 5-6 was considered to mean 'agree' and an IQR of ≤ 1.75 was considered indicative of consensus.

The Wilcoxon matched-pairs signed-rank test was used to assess stability of results. Results were deemed stable when there was no significant difference between statements (von der Gracht, 2012). A p value $P \leq 0.05$ was used in this study. Additionally data were provided on median and IQR values across rounds to provide additional information on stability of response.

The final protocol was developed through combining the case studies and identifying similarities between cases. Statements which appeared across case studies were included in the final protocol.

4.5.5 Ethics

The study was approved by London South Bank University Research Ethics Committee on 3.09.2013 (appendix 4.5). The questionnaire was piloted on five individuals in October 2013, the study commenced in November 2013 and completed in March 2014.

The study was deemed to be necessary and potentially beneficial to the wider society. All participants were provided with a participant information sheet which included details of the study, Delphi procedure and the researcher's expectations of the participants. The purpose of the study was clearly stated in the information sheet. All participants were advised to take time to decide if they wished to participate in the study and were free to contact the researcher by telephone or email to discuss the study prior to consenting to participate. Although participants were not provided with a formal consent form, it was clarified to participants that response by email was taken as consent to participate. Participants were made aware that the researcher and

supervisor would have direct access to information and complete anonymity was not guaranteed. However, anonymity between participants was guaranteed.

All data were confidential and stored securely on a password-protected PC and in locked filing cabinets. Only researchers involved in the study had access to data. Participants were assured of confidentiality. A coding system was developed to track respondents. All participants were given an identification number to allow the researcher to link responses, follow up non-responses and remove names from questionnaires. A filing system was developed which contained the participants' identification number and response to each round. Reminders or other information sent to participants were also recorded here. A master list of the participants' names and identification was developed and kept in a separately locked filing cabinet, away from other data. All hard copies of data were stored at London South Bank University in locked cabinets. Data stored on a computer was password protected.

Although participants were contacted throughout the study (thanking them for their participation and reminding them to complete the questionnaire) this was kept to a minimum to avoid participants feeling forced to continue and unable to withdraw from the study. It was not anticipated that the study would cause distress or harm to participants as the questionnaire was not about personal matters. However, participants were free to contact the researcher to discuss any concerns about the study.

Summary of Delphi methods

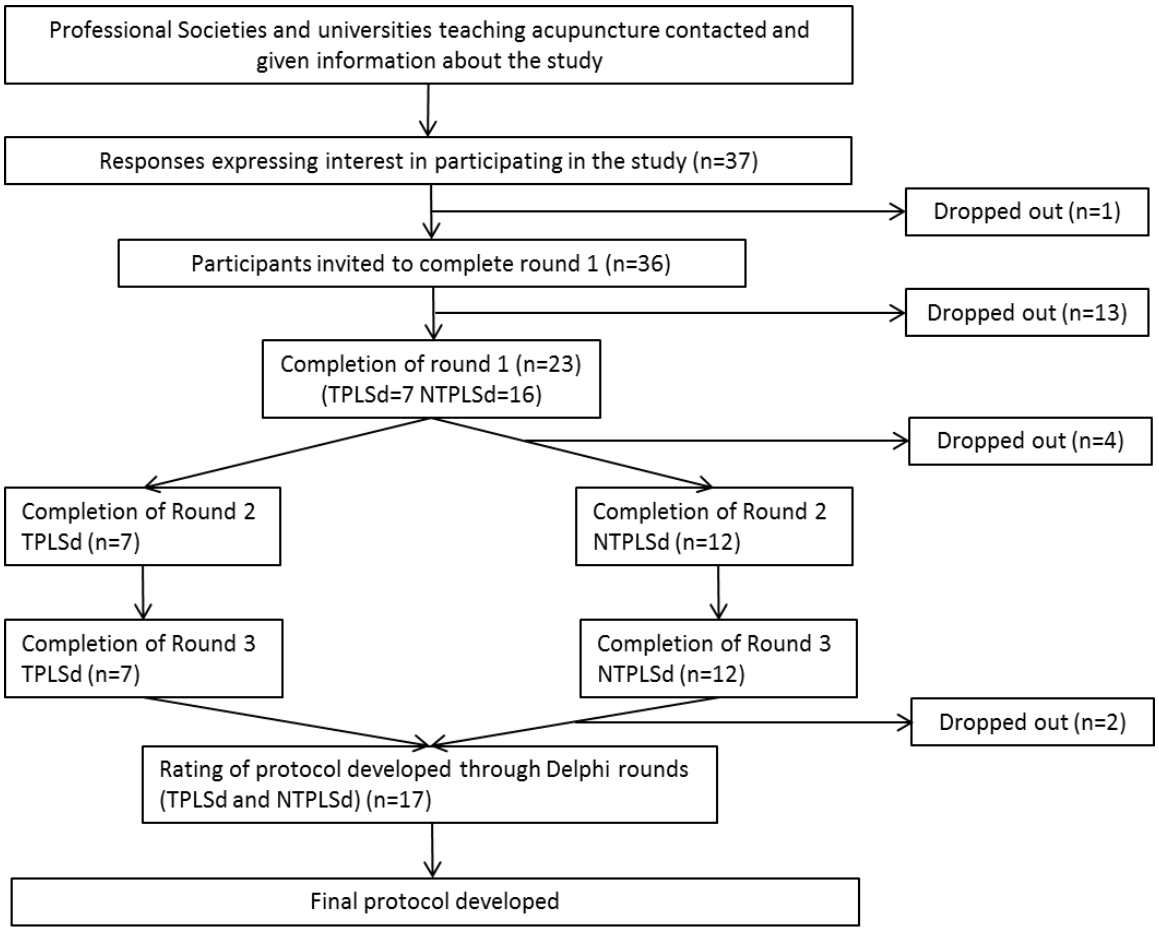
- A classical Delphi approach was taken.
- Two parallel studies were run; one included participants with past experience of treating PLSd and the other participants with no past experience.
- A six point Likert scale was used in round 2-4.
- A measure of variance (IQR ≤ 1.75) was used to define consensus, agreement was defined as a group median of 5-6. Stability of response was assessed using the Wilcoxon matched-pairs signed-rank test.

4.6 Results

A total of 37 practitioners initially expressed an interest in participating, of which 36 consented to participate. Of these 23 completed round one, of which 7 had past experience of treating PLSd, and 19 completed both rounds two and three (12 acupuncturists, 6 physiotherapists practicing acupuncture, 1 acupuncturist and physiotherapist). A total of 17 also ranked and 6 commented on the final protocol developed through the Delphi process. During the Delphi process 4 participants dropped out and 2 others did not rate or comment on the final protocol. The reasons for attrition by the 14 participants who did not complete round one was sought. A total of 12 responded stating; lack of time (n=7), lack of experience in treating PLSd (n=3), IT problems (n=2), being on holiday (n=1), missed deadline (n=2). Figure 4.5 shows participant flow through the Delphi process.

Table 4.4 shows participant demographics. The majority of participants were acupuncturists (n=13). No physicians practicing acupuncture participated in the study. All participants had completed acupuncture training in the UK and no participants had trained solely in China. Most participants practiced a combination of TCM and 5 Element acupuncture (n=6). A total of 4 participants used a combination of TCM and WMA, 4 practiced TCM style acupuncture only and 4 practiced WMA only. A combination of TCM, 5 Element and WMA was practiced by 2 participants, and 2 practiced TCM acupuncture along with other styles (including 5 Element, Western Medical, Korean Hand Therapy, Japanese, and Battlefield acupuncture). Only 1 practiced WMA and an 'other style'. In the TPLSd group 6 practiced TCM style acupuncture +/- other acupuncture styles and 1 practiced WMA. In the NTPLSd group 12 practiced TCM style of acupuncture +/- other acupuncture styles and those who did not practice TCM acupuncture practiced WMA +/- other acupuncture styles (n=4). In the TPLSd group, 6 were acupuncturists' ± physiotherapists and 1 was a physiotherapist. In the NTPLSd group, 8 were acupuncturists and 8 were physiotherapists.

Figure 4.5 Flow chart of participants through the Delphi study



Key: TPLSd, practitioners with past experience of treating phantom limb pain; NTPLSd, practitioners with no past experience of treating phantom limb pain.

Table 4.4 Delphi participant demographics

Participant Demographics		(n=23)	TPLSd (n=7)	NTPLSd (n=16)
Age	31-40 years	3	0	3
	41-50 years	10	4	6
	51+years	10	3	7
Gender	Male	8	4	4
	Female	15	3	12
Professional Background	Acupuncturist	13	5	8
	Physiotherapist practicing acupuncture	9	1	8
	Physiotherapist and TCM acupuncturist	1	1	0
Professional Membership	BAcC	12	5	7
	CSP (and AACP)	9 (5)	1 (1)	8 (4)
	BMAS	1	1	0
	Australian Natural Therapists Association	1	0	1
Place of study	UK	20	5	15
	UK and China	3	2	1
Years in Practice	0-5 years	5	0	5
	6-10 years	3	0	3
	11-20 years	11	5	6
	21+ years	4	2	2
Current time in clinical practice	PT	14	2	12
	FT	9	5	4
Area of speciality	Yes	16	5	11
	No	7	2	5
Style of acupuncture used	TCM	18	6	12
	WMA	12	3	9
	5 Element acupuncture	9	3	6
	Japanese acupuncture	2	0	2
	Battlefield acupuncture	1	0	1
	Korean hand therapy	1	0	1
	Other	1	1	0
Past experience treating PLP	Yes	7	7	0
	No	16	0	16

Key: TPLSd, practitioners with past experience of treating phantom limb pain; NTPLSd, practitioners with no past experience of treating phantom limb pain; BAcC, British Acupuncture Council; CSP, Chartered Society of Physiotherapy; AACP, Acupuncture Association of Chartered Physiotherapists; BMAS, British Medical Acupuncture Society; PT, part time; FT, full time; TCM, Traditional Chinese Medicine; WMA, Western medical acupuncture.

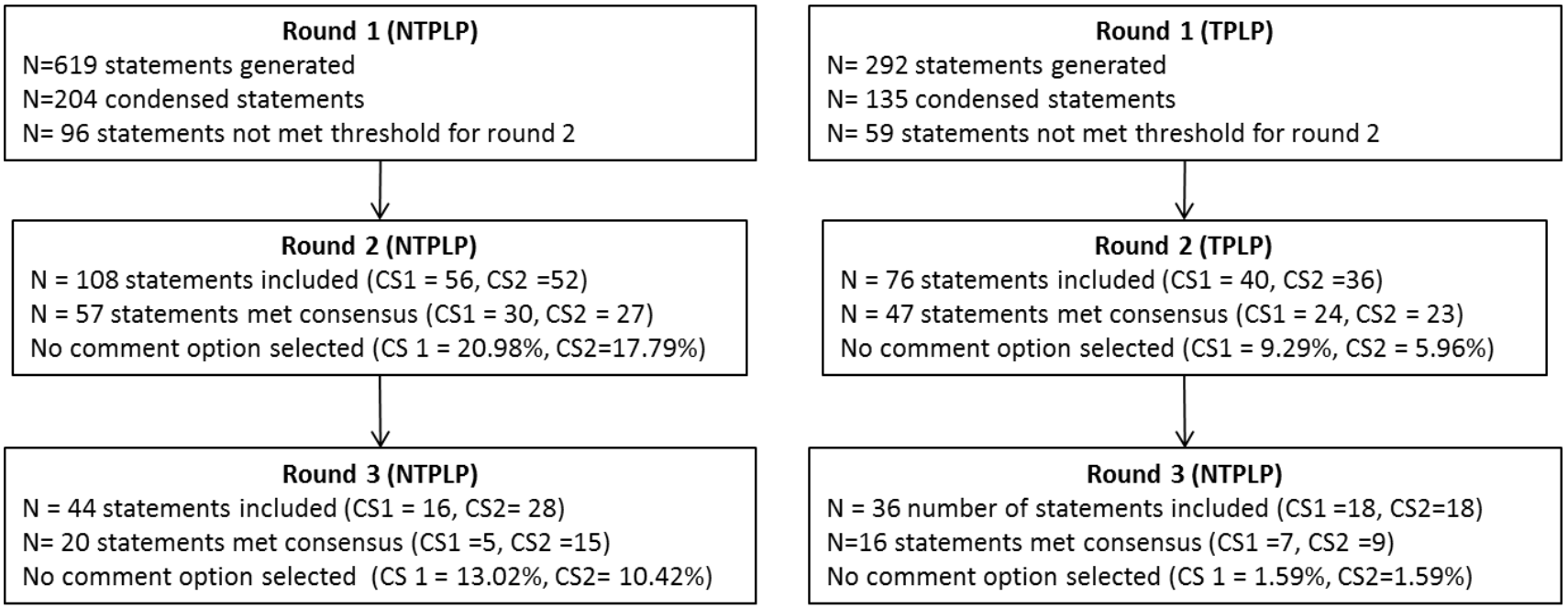
4.6.1 Statement generation and consensus

Figure 4.6 provides data on the number of statements included in each round and the number of statements meeting consensus throughout the rounds. In round one 619 NTPLSd and 292 TPLSd statements were generated which were condensed down 204 and 135 statements respectively. Of the condensed statements 96 were omitted in the NTPLSd group as they did not meet the threshold for inclusion in round two (only appeared once) and in the TPLSd group 59 were omitted for the same reason.

Of the statements included in round 2, 53% of NTPLSd statements and 62% of TPLSd statements met consensus and in round 3, 45% of NTPLSd statements and 44% of TPLSd statements met consensus. The 'no comment' option was selected <21% of the time in the NTPLSd group and <10% in the TPLSd group.

Table 4.5 provides data on questions which were included in round three. In the NTPLSd group 13 questions were included in round three (as less than 50% of ranked statements had met consensus or agreement had not been met). In the TPLSd group 9 questions were included (as less than 50% of ranked statements had met consensus or 50% consensus had been met but the question was recirculated to gain further consensus on point choice).

Figure 4.6 Numbers of statements generated and included in each Delphi round and number of statements meeting consensus



Key: TPLP, practitioners with past experience of treating phantom limb pain; NTPLP, practitioners with no past experience of treating phantom limb pain; CS1, case study 1; CS2, case study 2.

Note: *As ranked statements which had met consensus in round two were not omitted from questions which were recirculated in round three, the number of statements recirculated in round three is not the difference between statements which were included and met consensus in round two.*

Table 4.5 Delphi round 2 data on number of statements under each question which did / did not meet consensus and questions included in round 3

	NTPLSd						TPLSd					
Question	Number of statements met consensus		Number of statements not met consensus		Included in round 3 (Y / N)		Number of statements met consensus		Number of statements not met consensus		Included in round 3 (Y/N)	
	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2
1 What pathology / syndromes would you diagnose this patient with?	4	7	2	0	N	N	6	2	0	1	N	N
2 What would be your main treatment principle when treating this patient?	6	6	2	3	N	N	4	4	3	0	N	N
3 Would you use body, auricular or scalp acupuncture or a combination of any of these in the treatment of this patient?	0	0	2	2	Y	Y	1	1	0	0	N	N
4 If using body acupuncture which limbs would you needle?	1	0	2	2	Y	Y	1	1	1	0	N	N
5a What specific points would you use to treat the underlying pathology causing PLP in this case study and why (auricular)?	1	1	3	0	Y	N	3	4	0	0	N	N
5b What specific points would you use to treat the underlying pathology causing PLP in this case study and why (body)?	12	7	4	8	N	Y	6	7	7	7	Y	Y**
6 Would you try and obtain deqi when needling this patient?	1	1	0	0	N	N	1	1	0	0	N	N
7 How long would you retain the needles for?	1	0	1	2	N	Y	0	1	2	0	Y	N
8 Would you manipulate the needles during treatment and if so how frequently?	0	1	4	1	Y	Y*	0	1	1	0	Y	N

	NTPLSd						TPLSd					
Question	Number of statements met consensus		Number of statements not met consensus		Included in round 3 (Y / N)		Number of statements met consensus		Number of statements not met consensus		Included in round 3 (Y/N)	
	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2
9 Would you use electro acupuncture?	0	0	1	1	Y	Y	0	0	1	1	Y	Y
10 Would you use cupping, moxa or any other adjunctive treatment?	0	0	2	4	Y	Y	0	0	1	1	Y	Y
11 How often / frequently would you treat this patient?	2	3	1	1	N	N	1	0	0	2	N	Y
12 How many treatments would you anticipate giving in total for a course of treatment?	2	1	2	1	N	N	1	1	0	1	N	N
Total	30	27	26	25	-	-	24	23	16	13	-	-

Key: *included in next round as agreement not met (score <5); **included in next round as 50% not met consensus and researchers wanted clarity on consensus on point choice; CS1, case study 1; CS2, case study 2; NTPLSd practitioners with no past experience of treating PLP; TPLSd, practitioners with past experience of treating PLP; PLP, phantom limb pain.

4.6.2 Statements which met consensus and agreement

Post completion of round three statements had met consensus and agreement for 7/12 questions (for both case studies 1 and 2) in the NTPLSd group. In the TPLSd group, statements had met consensus for 8/12 questions (case study 1) and 10/12 questions (case study 2). The Wilcoxon matched-pairs signed-rank test showed good stability of results with no significant difference between rounds in 93.0% of NTPLSd statements and 97.2% of TPLSd statements. Scores for statements which met agreement and consensus are provided in appendix 4.6.

Across the case studies there was agreement and consensus on; the treatment principle to reduce pain and move qi and blood, to use the auricular acupuncture point Shen men, to either use local points or mirror the points on the contralateral limb, to try and obtain deqi, to treat at least six times in total. Across the case studies no consensus was met on whether to use electro-acupuncture, cupping, moxibustion or any other adjunctive treatments.

Comparison on the NTPLSd and TPLSd statements showed there were differences. The NTPLSd group included the treatment principle 'tonify the spleen' and did not meet consensus on whether to treat using body acupuncture or body and auricular acupuncture and on whether to treat both lower limbs or the contralateral limb only. The TPLSd group, however, achieved consensus on using auricular and body acupuncture on the contralateral limb. The NTPLSd group included the specific points LR3, GV20, SP10, 4 Gates (LR3 + LI4), GB34, PC6 whereas the TPLSd group only recommended LR3, GB34 and PC6. Only the NTPLSd group advised points on the lumbar spine (taking a segmental approach to dermatomal pain). The NTPLSd group recommended weekly treatment, reducing frequency as symptoms abated, whereas the TPLSd group recommended twice weekly treatments.

4.6.3 Devising a protocol

By combining the case studies and identifying similarities between cases a protocol was developed (figure 4.7). Statements which appeared across case studies were included in the final protocol. Bladder points in the lumbar / sacral area, GB34 and PC6

acupuncture points were not included in the protocol as they only met consensus in case study 2 so were considered not generalisable across the different cases studies.

The protocol was rated anonymously by 17 of the 19 participants who finished the Delphi process using the same Likert scale as used during the Delphi process (point 4.6.3). On asking 'how strongly do you agree or disagree with this protocol' 88.3% (n=15) agreed or strongly agreed with the protocol and 11.76% (n=2) somewhat agreed. No participants disagreed with the protocol.

Six participants provided feedback on the protocol. Feedback included that it was considered interesting and surprising that consensus was not met in all areas and that the protocol allowed room for manoeuvre. One participant stated that he/she would not use GV20 and another felt needle retention time was excessive. One participant felt using the point pair LI4 and LR3 bilaterally (Four gates) was problematic, and it was proposed that Yintang could be used to replace LR3 on the amputated limb. One participant felt the protocol should be referred to as guidelines. One participant took the protocol to a team meeting and feedback was that a protocol was not needed as each patient would present and should be treated as an individual.

> *"Pretty good outcome for a consensus process! However, it's interesting that consensus could not be reached on details of needle manipulation, EA and other adjunctive treatments - and also that the result is fairly general, with plenty of room for manoeuvre. Personally, I wouldn't use Du20, but that's just me." Quote 1.*
>
> *"I'm surprised that consensus was not met with electro-acupuncture." Quote 2.*
>
> *"I would try to avoid calling it a protocol, preferring to use Guideline." Quote 3.*
>
> *"I think that leaving the needles in for that long is excessive; the idea is to move Qi and Blood and to nourish Qi and Blood - in my experience the longer you leave the needles in the more draining it is of Qi and Blood." Quote 4.*
>
> *"I have a problem with 4 gates with an amputee as one gate is missing and would use Yintang as my 4th gate" Quote 5.*

"I have taken this to our acupuncture team meeting, which is attended by both traditional and western-trained acupuncture. The general feeling from this forum was that we don't really need a protocol for this sort of patient as each and every patient is assessed on their own merit. The traditional acupuncturists took quite an exception to the Qi and Blood stagnation diagnosis as they feel that every patient will present differently and would therefore need to be treated as such." Quote 6.

Figure 4.7 Acupuncture protocol for the treatment of phantom limb syndrome

Underlying Pathology:	• Qi and Blood Stagnation • Pathologies specific to the individual (as diagnosed during assessment)
Main Treatment Principles:	• Manage and reduce pain • Move qi and blood • Treat pathologies diagnosed during assessment which are specific to the individual • Reduce stress and calm the mind if necessary
Style of Acupuncture:	• Combination of body and auricular acupuncture
Limbs Needled:	• Opposite limb to amputation and possibly also the residual limb
Recommended Auricular Acupuncture Points:	• Shenmen (to calm the mind and reduce pain) • Sympathetic (to manage stress and anxiety) • Points corresponding to the lower limb
Recommended Body Acupuncture Points:	• Local points on the stump depending on the health of the tissue and the patients reaction • Mirroring local and distal points by needling them on the opposite limb • Points on the lower back taking a segmental approach to dermatomal pain • 4 gates (LI4 + LR3) (for pain relief and to improve stagnation and balance) • LR3 (liver 3) (to resolve stagnation, tonify yin and balance liver pathologies) • GV20 (governor vessel 20) (to lift the spirits, decrease stress and improve sleep) • SP10 (spleen 10) (to move blood)
Try and obtain deqi when needling:	• Yes
Needle retention time:	• 20-30 minutes
Needle manipulation during needle retention time:	• Consensus not met
Use electro-acupuncture:	• Consensus not met
Use of cupping, moxa or other adjunctive treatment:	• Consensus not met
Treatment frequency:	• Weekly or twice weekly and reduce frequency of treatment as symptoms abate
Total number of treatments:	• At least six (approximately 10)

Summary of Delphi results

- 19 participants completed all Delphi rounds (n=12 NTPLSd, n=7 TPLSd).
- 108 NTPLSd and 76 TPLSd statements were generated and circulated in round two.
- In round two, 53% NTPLSd and 62% TPLSd statements met consensus and in round three 45% NTPLSd and 44% TPLSd met consensus.
- Overall, statements met consensus and agreement for 7/12 questions (case studies 1 and 2) in the NTPLSd group and for 8/12 questions (case study 1) and 10/12 questions (case study 2) in the TPLSd group.
- The Wilcoxon matched-pairs signed-rank test showed good stability of results (no significant difference between rounds in 93.0% of NTPLSd statements and 97.2% of TPLSd statements).
- The protocol developed from the Delphi study was rated anonymously by 17 of the participants and 88.3% agreed or strongly agreed with it.

4.7 Discussion

4.7.1 Pathology and treatment principles

In all case studies participants achieved consensus on the pathology diagnosed and the question was not recirculated in round three. A wide range of items were listed suggesting that, as is common practice in CAM, participants diagnosed the individual case studies holistically taking the whole case into consideration. A common item listed across the case studies was 'qi and blood stagnation' suggesting that this pathology was specific to PLSd. Similarly, in all case studies there was consensus on the treatment principle to 'move qi and blood' and resolve pain. In TCM physical trauma (such as amputation) causes local stagnation of qi or blood in the area with a minor trauma causing stagnation of qi and a major trauma causing stasis of blood. Although the trauma may be transient, the effects of trauma can manifest for a long time with local stagnation of qi, blood or both in the affected area. Clinical manifestations of qi stagnation include distending pain that moves from place to place and blood stagnation includes pain which is boring, fixed and stabbing in character (Maciocia, 2005) suggesting a mixture of both qi and blood stagnation may contribute to PLSd.

4.7.2 Style of acupuncture

No participants had trained solely in China and only three had completed any form of training in China. This may have an influence on results as there are differences in style of acupuncture treatment practiced in China and the UK. Notably, as reported in appendix 2.5, on review of English and Chinese studies documenting acupuncture treatment for PLSd, Chinese studies tended to use a combination of body and scalp acupuncture, whereas English studies tended to use just one style and not use scalp acupuncture (Hu *et al.*, 2014a). No controlled trials have assessed whether a combination of styles of acupuncture or one style alone is more effective (Hu *et al.*, 2014b). Unlike in China, scalp acupuncture is not commonly taught or practiced in the UK and in this study no scalp acupuncture points were recommended by participants in round one. As the study aimed to develop an acupuncture protocol which could be used in the UK, the lack of participants who had completed training in China and lack of recommendation of scalp acupuncture points was not seen as a limitation of the study.

In the TPLSd group consensus was achieved recommending using a combination of body and auricular acupuncture. However, in the NTPLSd group consensus was not met in either case study. This may be due to participants' background and training. Some participants may not have had training in auricular acupuncture, causing lack of consensus on its usage. On review of English published case studies on PLSd, none documented using a combination of both auricular and body acupuncture and it is not clear whether auricular, body or a combination of these approaches is most efficient for treating PLSd (Hu *et al.*, 2014a). However, in clinical practice it is common to use a combination of body and auricular acupuncture, so results of this study are not unusual. A systematic review suggests auricular therapy may be effective for the treatment of pain (Asher *et al.*, 2010) further supporting including auricular acupuncture within the proposed protocol.

In the TPLSd group consensus was achieved, recommending treating the contralateral limb. In the NTPLSd group consensus was not achieved in round 3, possibly due to participants' lack of experience in treating this condition. However, consensus was achieved in case study 1 round 2 to treat both lower limbs (median = 5, IQR = 0.75). It is unclear why this item met consensus in round 2 but then did not meet consensus in round 3. Case studies and trials on amputees with PLSd do tend to recommend treating the contralateral limb (Hu *et al.*, 2014a, Hu *et al.*, 2014b) but there are reports published which treat the residual limb (Xing, 1998). Treating painful conditions by giving acupuncture to the contralateral side is a recognised treatment approach which is advised in the ancient Chinese Text the Neijing Suwen (Maoshing, 1995) and is known as "juci" (implanting a needle on the opposite side of the body to the disease or disorder to treat it). It is useful when ipsilateral needling is not possible due to contraindications, trauma, anomaly and post-amputation (Miura *et al.*, 2007). Laboratory studies have compared the efficacy of ipsilateral to contralateral acupuncture and found that the degree of effectiveness is similar (Miura *et al.*, 2007, Yi *et al.*, 2011). Clinical studies have found that both ipsilateral local needling and contralateral distal needling can reduce carpal tunnel syndrome (Maeda *et al.*, 2013) and a systematic review suggests contralateral needling may be superior to ipsilateral needling in post-stroke rehabilitation (Kim *et al.*, 2010). Spinal interneurons may have an important role in reducing pain through contralateral needling (Bileviciute-Ljungar *et al.*, 2001). In the

proposed protocol, contralateral needling was advised but an option to treat the residual limb was also included as recommendations met consensus which involved needling the residual limb.

4.7.3 Acupuncture points

Auricular acupuncture points which met consensus across case studies included Shenmen, Sympathetic and points relating to the lower limb. Shenmen is commonly used in the treatment of pain and in Asher *et al.* (2010) systematic review on auriculotherapy for pain management, this was the most commonly included point. Ear and scalp acupuncture techniques are commonly used by the American military Service to reduce the pain associated with battlefield wounds including PLSd (Niemtzow *et al.*, 2006). Battlefield acupuncture involves auricular acupuncture to five areas of the ear which are linked to the sympathetic nervous system and areas of the brain including the thalamus and cingulate gyrus. Mechanism of action involves the modulation of pain processing in cortical centres (Plunkett *et al.*, 2012). Battlefield acupuncture includes the auricular points Cingulate Gyrus, Point Zero, Shenmen, Omega 2 and the Thalamic point (Niemtzow *et al.*, 2006) and a pilot study has shown Cingulate Gyrus and Thalamic point to be effective in reducing acute pain (Goertz *et al.*, 2006). However, of these points only Shenmen met consensus in this protocol. The auricular point Sympathetic may also have met consensus in this study because it balances activity in the sympathetic and parasympathetic branches of the autonomic nervous system, aids relaxation, has a strong analgesic effect and promotes blood circulation (Landgren, 2008).

Of the body acupuncture points many were suggested and of those which met consensus some were related to the holistic treatment of the specific case study and were not specific to treating PLSd. However, there were points which were included in both case studies (case study 1 and case study 2) suggesting these points were chosen specifically for treating PLSd. Both LR3 (Taichong) and the four gates (LR3 + LI4) met consensus across case studies. LR3 was also found to be the mode point used in the narrative review (appendix 2.5), followed by LI4 (Hegu) (Hu *et al.*, 2014a). In TCM LR3 promotes the smooth flow of liver qi, invigorates blood, calms the mind (reduces irritability and worry due to emotional stress) and calms spasms (Maciocia, 2005). In

clinical practice LR3 is commonly combined with LI4 as the four gates to enhance the calming effect on the mind and stop pain (Maciocia, 2005). The four gates comprise of the gates of qi on the yang ming channel and the gates of blood on the jue yin channel. Pairing the points moves both qi and blood throughout the body (Ju-Yi and Robertson, 2008). As qi and blood stagnation was considered an underlying pathology of PLSd and as all case studies met consensus on the treatment principle to move qi and blood and resolve pain, review of the function of these points explains why they met consensus and were recommended in both case studies. SP10 (Xuehai) also met consensus across case studies and was included in the final protocol. Like the four gates, SP10 the 'Sea of Blood' invigorates blood and moves stasis (Maciocia, 2005).

One of the treatment principles included in the final protocol was to reduce stress and calm the mind. GV20 (Baihui) met consensus across the different case studies to lift the spirits, decrease stress and improve sleep. The point is situated at the vertex of the head (the place of maximum potential energy) and also the convergence of all the yang channels. The points lifting action on yang has a mental effect by rising clear yang to the brain and mind, thereby lifting depression and clearing the mind (Maciocia, 2005). Other points which met consensus in individual case studies (but not across case studies) for their calming effect included HT7 (Shenmen), PC6 (Neiguan) and Yintang. The main action of HT7 is to calm the mind when there is anxiety and worry under stressful conditions (Maciocia, 2005), PC6 has a powerful calming action on the mind both directly and indirectly (through it being part of the jue yin) (Maciocia, 2005) and Yintang is an extra point which is commonly used to calm the mind and relieve anxiety and insomnia (Maciocia, 2005). Although consensus was only met across case studies on GV20, it is recognised that in clinical practice other points such as these could be used to relieve stress and anxiety.

Local acupuncture points may have met consensus and been included in the protocol because practitioners practicing WMA commonly use neuro-anatomical principles when selecting acupuncture points to use and choose points which are in close proximity to the injured area with the intention of inducing a strong segmental pain inhibitory effect (Bradnam, 2003). Needling close to the injured tissue has the potential to elicit strong analgesic effects and encourage peripheral neuropeptide release producing local

vasodilatation and modulating the local immune response (Bradnam, 2003).

The NTPLSd group advised needling points on the lower back, taking a segmental approach to dermatomal pain. This was not mentioned in the TPLSd group, possibly as this approach to treatment is a western approach (in the TPLSd group 6 of the participants were acupuncturists practicing TCM style acupuncture and may not have had training in WMA). WMA is based on anatomy, physiology and pathology, and treatment of pain is based on the practitioners' impression of the predominant pain mechanism (Bradnam, 2003). Distant points can be used to avoid using too many local points (Bradnam, 2003) and points may be chosen because they are segmentally linked to the presenting condition (White, 2009). Points in other muscles or tissues sharing an innervation with the injured tissue or close to the spinal level that shares innervation with the injured part are chosen to influence the segment via the dorsal rami (Bradnam, 2003).

On comparing points which met consensus in case study two across the TPLSd and NTPLSd group, GB34 (Yanglingquan) PC6 and bladder points in the lumbar sacral area were recommended by both groups. These points may have been recommended because PC6 (as stated earlier) has a calming action on the mind, GB34 is the hui / influential point for sinews and can relax muscle cramps and spasms and invigorates the circulation of qi and blood in the legs (Maciocia 2005) and bladder points in the lumbar sacral region may have been recommended as local or segmental points.

4.7.4 Deqi, needle retention and needle manipulation

Consensus was met across all case studies advising to obtain deqi and to retain needles for 20-30 minutes. This was in keeping with acupuncture trials treating PLSd (Hu *et al.*, 2014b) and was not unexpected as many acupuncture textbooks recommend needle retention for this period of time (Ju-Yi and Robertson, 2008). According to the fundamental doctrinal source of acupuncture (Huang Di Nei Jing, Ling Shu Chapter 15) qi circulates through the meridians 50 times a day with one cycle of qi throughout the body taking 28 minutes and 48 seconds (Jing-Nuan, 1993). Needles should be left in to allow for a complete cycle of qi. Some styles of acupuncture such as 5 Element Acupuncture tend to recommend different needle retention times. In 5 Element

Acupuncture needles are not usually left in place when a patients qi is being tonified and when using sedation techniques needle retention time depends on pulse change. However, usual period of retention is advised to be around 20 minutes (Hicks *et al.*, 2004). Some texts recommend that the underlying pathological conditions decide duration of needle retention but also recommend in general that needles are retained for 15-20 minutes (Xinnong, 1999). Surprisingly in the narrative review (appendix 2.5) needle retention time varied from 30 seconds to 3-4 days with the majority of papers reporting 30-40 minutes (Hu *et al.*, 2014a). In clinical practice, needle retention time may vary depending on style of acupuncture being practiced and needle technique involved. When treating elderly or constitutionally weak patients, needle retention time may be shortened to avoid adverse effects such as nausea and fainting. These possibilities may not have been picked up in this study.

No consensus was met on needle manipulation. This may be because needle manipulation can vary even between different acupuncture points within the same treatment. Practitioners may provide different frequency and type of needle manipulation to different points within a single treatment depending on their intent and the specific function of each acupuncture point. Frequency of needle manipulation may depend on whether the practitioner is trying to tonify or sedate the area and the sensitivity and constitution of the patient. The specific type of needle manipulation can influence whether the point is tonified or drained; awaiting the arrival of qi by holding the needle is considered tonifying whereas guiding the qi can have a sedating effect (Ju-Yi and Robertson, 2008). Methods for moving qi may include flicking the needle, scratching the handle of the needle, pressing (grasping the needle firmly and turning it slowly with conviction), flying technique (similar to flicking the needle), twirling the needle or lifting and thrusting (Ju-Yi and Robertson, 2008). Neither frequency nor type of manipulation was established in this study.

4.7.5 Other treatment considerations

Across all case studies no consensus was met on whether to use electro-acupuncture or some other form of adjunctive treatment and there was minimal convergence between round 2 and round 3 with these statements. This may be due to participants' familiarity with different treatment techniques. Practitioners who use electro-acupuncture and

adjunctive treatments within their clinical practice may advise using them whereas participants with no experience may not. The use of electro-acupuncture and adjunctive treatments may depend on patient response, possibly being used as a treatment progression, and if this is the case it would be difficult to give a definitive yes or no answer as required in this study. Adjunctive treatments, including electro-acupuncture and moxibustion, are rarely used in conjunction with acupuncture to treat PLSd (Hu *et al.*, 2014a).

Consensus was met on treating weekly or twice weekly, reducing the frequency of treatments as symptoms abate and treating in total at least six and approximately ten times. In China acupuncture treatments for PLSd are often administered more frequently with treatments commonly administered daily for 10-30 treatments, whereas the UK tend to treat less frequently (weekly) and provide fewer total number of treatments (4-7) (Hu *et al.*, 2014a). This may be due to different educational backgrounds, cultural expectations and differences in healthcare systems and policy. In this study consensus on treatment frequency and total number of treatments was similar to UK case studies published on acupuncture treatment for PLSd.

4.7.6 Consensus and attrition

As stated earlier (section 4.4.3) there is no agreement in the literature defining criteria to use to determine consensus and in this study neither consensus nor stability of results were used as stopping guidelines. Consensus may be a contentious component of Delphi studies due to controversy in understanding the term, which can mean group opinion, general agreement or group solidarity in sentiment and belief (von der Gracht, 2012). IQR is generally accepted as an objective and rigorous way of determining consensus and as stated earlier an IQR of ≤2 on a 10 unit scale or ≤1 on a 4-5 unit scale is considered a suitable indicator of consensus (von der Gracht, 2012). An IQR of ≤1.75 as used in this study may have been a slightly large indicator of consensus but was chosen to avoid participant fatigue.

It has been remarked that consensus is meaningless if group stability has not been reached (von der Gracht, 2012) and both consensus and stability were recorded in this study to give an indication of both level of consensus and reliability of results. However,

only statements from 22 of the 48 questions were recirculated in round three so stability of results was only assessed for 46% of the total number of questions. Ideally all statements would have been recirculated in round three to gain a more thorough picture of stability of response but due to the large number of statements generated this was not done. The Wilcoxon matched-pairs signed-ranks test found responses to be stable and this should be a good indicator of stability of response for Likert scale, ordinal / ranked data.

Delphi technique is renowned for high attrition levels as it requires time and effort over a period of time from participants (Keeney *et al.*, 2011) and high levels of attrition can lead to response bias. Respondents with extreme views are more likely to drop out of Delphi than those with moderate views suggesting consensus may be in part due to attrition (Rowe and Wright, 1999). However, in this study post commencement of the Delphi process attrition levels were low, with only 4 dropping out after round one and 2 not rating the final protocol. This is unusual and the response rate usually reduces as rounds progress (Rankin *et al.*, 2012). The low level of attrition may be due to participants being within their scope of practice, being well informed on the commitments of the Delphi process prior to commencement of the study, regular contact being made with participants during the study process and a quick turnaround of results and rounds (each round was sent out four weeks after the previous round).

4.7.7 Protocol

Both the TPLSd and NTPLSd group produced similar items which met consensus across the two case studies. Notable differences between the two groups were that in the NTPLSd group consensus was not met on whether to use body acupuncture, auricular or a combination of both or whether to treat the ipsilateral, contralateral or both lower limbs. In the TPLSd group consensus on body acupuncture point use was only met on mirroring points whereas the NTPLSd group met consensus on 6 body points and this may be due to there only being 7 participants in the TPLSd group. The final protocol developed was not rigid and provided scope for practitioners to treat patients pragmatically and individualise treatment. Although the researcher felt the protocol was in keeping with the underlying principles of TCM and feedback was generally positive, feedback from one participant identified that some practitioners took ‘quite an

exception' to the protocol. This suggests some practitioners may be unwilling to use these guidelines. Practitioner willingness to use the protocol would need to be established before agreeing to participate in a RCT.

Summary of Delphi discussion

- Qi and blood stagnation may be an underlying pathology of PLSd.
- Although a combination of body and auricular acupuncture is not frequently reported in case studies, auricular acupuncture is effective for treating pain conditions, supporting the inclusion of this technique in the protocol.
- Contralateral needling is recognised in ancient Chinese medical texts, and has been shown to be an effective treatment for various pain conditions, suggesting it could be beneficial in the treatment of PLSd.
- Battlefield auricular acupuncture points may be appropriate for treating PLSd.
- Point choice may vary, depending on participant background, with Western Medically trained practitioners choosing points close to the spinal level that shares innervation with the injured part.
- Needle retention time established in this study is similar to text book guidelines.
- Consensus may not have been met on needle manipulation due to the large number of variations of technique which can be applied even within one treatment.
- The lack of consensus on the use of adjunctive treatments and electro-acupuncture may be due to participants' past training.
- Consensus on frequency of treatment and total number of treatments is in keeping with UK case studies treating PLSd with acupuncture.

4.8 Limitations and methodological considerations

A major limitation was that the study only recruited 7 practitioners with past experience of treating PLSd, and not ≥8 as aimed for (section 4.6). Also, although one practitioner specialised in chronic pain management / complex pain, no practitioners specifically specialised in treating PLSd. This is probably due to acupuncture not being a commonly used intervention for the treatment of PLSd. In past surveys, amputees have not reported using complementary and alternative therapies that require a practitioner (Ketz, 2008) and in a survey by Hanley *et al.* (2006) only 1% of amputees reported having ever used acupuncture (this was however an American study).

It is recognised that even though 7 participants had past experience in treating PLSd they were not necessarily experts in this field. Also, as stated earlier (section 4.4.1), the question of how an expert is defined and whether expert opinion is distinguishable from anyone else, is largely unresolved. In this study no criteria was set to define an expert and to avoid misleading terminology, no participants were defined as experts. Results therefore do not claim to represent expert opinion. This may reduce the validity of results. However, results and the protocol developed should represent 'good practice'.

The majority of participants in the TPLSd group were professional acupuncturists whereas in the NTPLSd group half were physiotherapists (with a western medical background) practicing acupuncture. WMA approach does not involve traditional concepts. Clinical effects on pain may be described through concepts such as Melzack and Walls gate theory (section 2.3) where acupuncture is considered to inhibit nociceptor function through stimulation of mechanoreceptors at the needle insertion point (Goertz *et al.*, 2006). Through including professionals with both western medical and traditional acupuncture backgrounds, the protocol included a mixture of acupuncture styles. However, as the study aimed to capture a broad approach to treatment including expertise from different disciplines, this was not seen as a limitation to the study.

Round one questionnaire did not capture information such as specific needle technique (tonify / sedate), depth of needle insertion and whether duration of needle retention would be the same for all points during treatment. It was not clear from round one

whether when mirroring points on the contralateral limb, channel pairing would be taken into consideration (for example treating the GB meridian for pain felt along the LR meridian). These areas need to be explored in future studies.

Potentially useful information was lost by introducing a threshold for inclusion of statements in round two. This meant that although the subjective view of outliers in round 1 may have raised important considerations, these were omitted from round 2. However, due to the large number of statements generated in round one (NTPLSd=619, TPLSd=292) this process of reduction was deemed necessary. Had fewer statements been generated in round one, all items would have been included in round 2. Future studies may benefit from having a more specific first round to avoid generation of large numbers of statements.

This study allowed information to be exchanged between individuals who were too geographically dispersed to meet face to face. However, Delphi studies have the limitation of diminishing the positive aspects of face to face exchange. Lack of face to face discussion meant reasons for disagreement could not be debated and this may have contributed to lack of consensus in certain aspects of the study such as whether to use electro-acupuncture and other forms of adjunctive treatment.

This study elicited valid opinion from professional acupuncture practitioners. However, Delphi technique does not produce right or wrong or definitive answers (Keeney *et al.*, 2011). It is recognised that although consensus was obtained for the majority of questions in this study, consensus is not the same as the correct or best and results of the study should be interpreted as such. The protocol developed in this study is not necessarily 'best practice' and is opinion only from the group of participants involved in this study. However, as the protocol was developed systematically through practitioners with a recognised training and three or more years of clinical experience, it could be interpreted as 'good practice'. As currently there are no recommended treatment guidelines for treating PLSd with acupuncture, this protocol should provide guidance on possible treatment.

4.8.1 Methodological considerations

Delphi studies fall into the debate of whether qualitative or quantitative quality appraisal criteria should be used. In this study the criteria of reliability and validity were used. This criterion was adhered to because: (1) Data were not collected in a 'real-world' setting but through on-line questionnaires which did not involve close contact between the researcher and participants, (2) A deductive, reductionist approach was taken throughout the study including during the analysis of qualitative data, (3) QCA is closely related to quantitative content analysis and therefore positivist criteria should be used to avoid cutting QCA off from its roots (Schreier, 2012), (4) Directed QCA involves researchers having prior theory which is supported and extended, meaning researchers are not working from the naïve perspective often associated with interpretivist designs (Hsieh and Shannon, 2005).

External reliability, the level of replication that could be expected if a similar study was undertaken (Lewis and Ritchie, 2003), was not tested and a test-retest procedure over different timeframes was not implemented. Internal reliability, the extent to which ratings internal to the research are replicable (Lewis and Ritchie, 2003) was ensured during round one through a code-recode procedure and through use of a second coder and in subsequent rounds through measuring stability of response. Reliability was also ensured through providing detailed information on the research process.

A Classical Delphi approach was taken to ensure validity of the study design. As Delphi results stem from group opinion which can be reviewed and judged, content and face validity could be assumed (Keeney *et al.*, 2011). Triangulation of results across groups enhanced validity. Validity may have been reduced because no criteria were provided to define experts and participants did not make up an 'expert panel'. However, as the inclusion criteria included a recognised acupuncture qualification and clinical experience, content validity may be assumed. Validity may also have been reduced due to the encompassing definition of consensus (IQR ≤ 1.75). During first round analysis, validity may have been reduced due to researcher interpretation and bias. Peer debriefing aimed to minimise this as did iteration and participant feedback from subsequent rounds (Keeney *et al.*, 2011). Round one created a large number of statements meaning lengthy subsequent rounds. This may have predisposed

participants to answer with lack of thought and accountability, so reducing validity. Participants may have been influenced by results from the group and altered their opinion accordingly.

As the study included participants from different professional backgrounds (acupuncture and physiotherapy) and participants in the study practiced a range of styles of acupuncture, the results of the study should be generalisable to both acupuncturists and physiotherapists and to practitioners practicing different styles of acupuncture.

4.9 Conclusion

This study did achieve all its objectives (except on the development of consensus on the use of adjunctive treatments) and a protocol was developed for the management of PLSd in lower limb amputees. Practitioners' views on the pathology and treatment of PLSd were established and a protocol suggested. Results of this study were used to guide the development of the feasibility study described in Chapter 6.

The protocol developed in this study is novel and provides guidelines which have not been previously available for acupuncture treatment of PLSd. The proposed protocol is not claiming to be the best or the most correct approach to treatment but does give some guidelines on which to base treatment and could be considered good practice. The protocol allows a pragmatic approach to treatment which is in keeping with TCM whilst still providing a structure to treatment. This is in keeping with the theoretical framework of the project; the MRC framework for complex intervention advises interventions should be both reproducible and workable in everyday practice (Craig *et al.*, 2008a). Further study is required to gain consensus on areas such as needle manipulation, use of electro-acupuncture and other adjunctive treatments and use of channel pairing when mirroring points on the contralateral limb.

Summary of Delphi conclusion

- The objectives of this study were achieved (except on developing consensus on the use of adjunctive treatments) and an acupuncture protocol was successfully developed for the treatment of PLSd.
- The protocol did not claim to be the best or most correct approach to treatment but provides 'good practice' guidelines not previously available.
- The protocol was used in the development of the feasibility study described later in the thesis.

Chapter 5. Exploring the acceptability of acupuncture intervention within the context of living with phantom limb syndrome and identifying outcome measures for use in a feasibility study

5.1 Introduction

PLSd is a prevalent complication post amputation which is poorly managed and little explored. During the qualitative literature search undertaken in Chapter 2, exploring the experience of PLSd, papers identified were of poor methodological quality or not transferable to a UK demographic population. This established the need for further research in this area. Better understanding of the experience of PLSd was considered a necessary part of this project to help the researcher have a better understanding of PLSd and to identify if the feasibility study was relevant. Additionally, whilst completing the qualitative review, no papers were identified exploring the acceptability of acupuncture and studies evaluating the effectiveness of acupuncture did not provide data on the perceived acceptability of this intervention.

This study was considered necessary to gain understanding of amputees' experience of PLSd. It was also considered necessary to establish preliminary information on amputees' perceived acceptability of an acupuncture intervention whilst receiving a routine NHS care package before conducting a feasibility study. The author also wanted to establish if participating in a RCT was perceived acceptable and for amputees to be involved in the decision making process of the inclusion and exclusion of potential outcome measures which could be used in a future feasibility study. These were all considered important aspects of the developmental stage of a complex intervention.

This chapter explores the perceived acceptability of acupuncture, within the context of living with PLSd and identifies potential outcome measures which could be used to evaluate the effectiveness of acupuncture in a feasibility study. The choice of study design, a qualitative cross-sectional descriptive study, and its place within the overall MMR project is justified. Framework analysis is discussed and the specific methods used, results obtained and a discussion of findings is presented. In keeping with

qualitative research, during quality appraisal the criteria trustworthiness; credibility, dependability, transferability, confirmability were used. Findings from this study have been published and are included in appendix 5.1.

5.2 Objectives

This chapter addressed the project objective described in the introduction (figure 1.1):

- Explore lower limb amputees' perceived acceptability of acupuncture within the context of living with PLSd, appropriateness of outcome measures and willingness to be involved in a randomised controlled trial.

As described in the introduction (figure 1.2) the component parts of this objective were to:

- Establish the perceived acceptability of acupuncture intervention for the treatment of PLSd.
- Explore the experience of PLSd in lower limb amputees.
- Identify potential outcome measures to be used in a feasibility study.
- Establish if amputees would be willing to participate in a feasibility study.
- Explore if amputees feel they are provided with adequate information about PLSd.

5.3 Situating the research

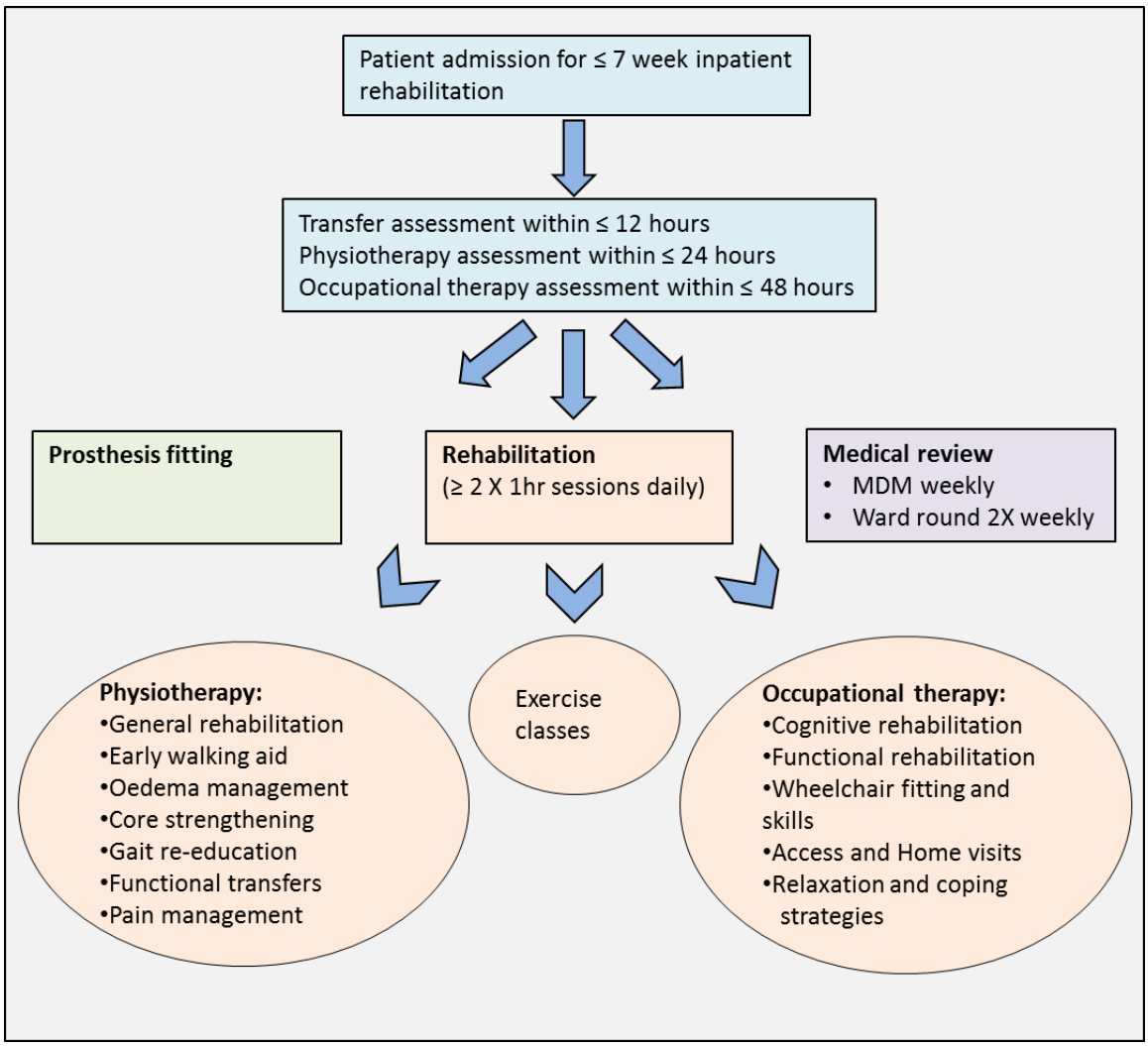
The study was considered part of the overall MMR approach of this project, a multiphase design, as findings from this study informed the design of the feasibility study (Creswell and Plano Clark, 2011). Additionally, this study fitted with the framework used in this project, the MRC framework for developing and evaluating complex interventions, which recommends thinking about implementation and if necessary spending time completing new primary research before conducting a feasibility / pilot study (Craig *et al.*, 2008a).

This study was deemed a necessary stage in the project, as in keeping with the MRC framework for developing and evaluating complex interventions, the researcher needed to gain understanding of PLSd and obtain preliminary data on the perceived acceptability of acupuncture and being involved in a RCT before conducting a feasibility study. The study aimed to explore the acceptability of acupuncture and allow amputees to be involved in the choice of outcome measures used in the feasibility study described in Chapter 6. Within this, the study explored the wider issues surrounding PLSd, such as personal experience, to ensure the feasibility study was relevant. The researcher did acknowledge that acceptability of acupuncture would not become fully apparent until conducting the feasibility study.

The research was conducted at an amputee rehabilitation unit (ARU) in London. The unit was a 12 bedded inpatient centre providing up to seven weeks of specialist rehabilitation for adults who had undergone major amputation. The unit brought together evidence based, post-operative amputee care and provided amputees with access to specialist medical, nursing, therapy and counselling interventions. Staff at the ARU included; medical consultant, nursing staff, physiotherapists, occupational therapists, prosthetist, social worker, counsellor, rehabilitation assistants, pharmacist, vascular nurse specialist and a chaplain. Patient care pathways at the ARU included a ward round twice weekly, prosthesis fitting, and rehabilitation sessions at least twice daily, including physiotherapy, occupational therapy and / or exercise classes. Counselling was not provided routinely. The unit aimed to return patients to functional independence and facilitated early mobilisation, prosthetic provision and psychological care. Patient care pathways at the unit are shown in figure 5.1.

The ARU accepted both primary and established amputees who had undergone a functional decline but not those who were medically unstable, had wounds which prevented commencement of rehabilitation, required specialist or respite care or those waiting for a social service care package.

Figure 5.1 Patient care pathways at the amputee rehabilitation unit



Key: MDM, multi-disciplinary team meeting.

5.4 Methodological stance

5.4.1 The 'pragmatic qualitative research' approach

Savin-Baden and Howell Major (2013) identify a qualitative research approach called 'pragmatic qualitative research' and this was used in this study. Pragmatic qualitative research is a methodology which aligns with pragmatism, the philosophical position taken in this project. Although pragmatic qualitative research usually falls somewhere between a purely descriptive or interpretive approach, researchers using this methodology can situate their research anywhere along the objective – subjective continuum. In this study the relatively objective type of pragmatic qualitative research taken was 'qualitative descriptive study' as described by Sandelowski, (2000).

Qualitative descriptive studies use practical methods to answer a research question and provide a comprehensive summary of an event in everyday terms. It is appropriate when researchers want to provide a descriptive account from an interpretive perspective and aims to provide a description of an event or an experience as interpreted by the researcher (Savin-Baden and Howell Major, 2013). Despite taking an interpretive approach, these studies stay close to the data, do not use a highly abstract framework and provide a straight descriptive summary of the data (Sandelowski, 2000). It is relatively unacknowledged compared to other designs such as phenomenology and ethnography but allows for a comprehensive summary of a phenomenon (Sandelowski, 2000). As this study aimed to give a descriptive summary of the perceived acceptability of acupuncture within the context of amputees living with PLSd, this approach was deemed appropriate.

Using a qualitative descriptive study design aligned with pragmatism, the philosophical underpinning of this project, adopting an open orientation to the study and drawing on a range of methods all served to answer the research question (Savin-Baden and Howell Major, 2013). Using a qualitative descriptive methodology allowed the researcher to take an elective approach and use a range of different methods to find the most appropriate way of answering the research question. However, although qualitative descriptive studies allow researchers the freedom to use the methods which work best, they do have specific characteristics as described below.

Qualitative descriptive studies often involve individuals and typically view people as the primary data source (Savin-Baden and Howell Major, 2013 and Sandelowski, 2000). Researchers are not required to spend extensive time in the field but research should be conducted in its natural environment (Savin-Baden and Howell Major, 2013). Data are usually collected through interviews or focus groups, but may also use observation and documentary analysis (Sandelowski, 2000). The three fundamental types of research interviews are structured, semi-structured and unstructured. Qualitative descriptive studies favour semi-structured and unstructured interviews (Sandelowski, 2000). Studies which have a strong sense in advance of the issues that need exploring may use semi-structured interviews whereas exploratory studies may use unstructured interviews (Arthur and Nazroo, 2003). Interviews may take a thematic, biographical, topic-centred or narrative approach (Mason, 2002) and the philosophical underpinning of the research influences the interview.

Qualitative descriptive studies try to gain perspectives from many different types of participants, and in keeping with this use purposive sampling techniques, especially maximum variation sampling (Savin-Baden and Howell Major, 2013 and Sandelowski, 2000). This method is preferred as it allows researchers to explore common and unique manifestations of a target phenomenon across a broad range of diverse cases generating information rich data (Sandelowski, 2000). Although the purposive sampling criteria may change during a study (Creswell, 2007) it can be set *a priori* and a sample matrix and quota developed before commencement of a study (Ritchie *et al.*, 2003a).

As all types of pragmatic qualitative research recognises that findings are an interpretation of the researcher (Savin-Baden and Howell Major, 2013), reflexivity on the role of prior assumptions and experience of the researcher is required (Pope and Mays, 2006). This can help the researcher consider their position and influence on the study and positions them as an integral and integrated part of the research (Savin-Baden and Howell Major, 2013). Reflexivity enhances confidence in the research and establishes credibility (Walker *et al.*, 2013). Reflection can happen in advance of the study, during the study through field notes and a reflective diary and retrospectively.

5.4.1.1 Data analysis

Pragmatic qualitative research uses inductive approaches to data analysis, such as qualitative content analysis and thematic analysis (Savin-Baden and Howell Major, 2013) and qualitative descriptive studies recommend using qualitative content analysis. In this study, framework analysis was used because it was considered best suited to analysing the type of data generated; cross-sectional descriptive data (Smith and Firth, 2011), semi-structured interviews (Gale *et al.*, 2013), research which has specific questions, a pre-designed sample and *a priori* issues (Srivastava and Thomson, 2009), research which tends to be focused (Smith and Firth, 2011) and data which are not highly heterogeneous as data needs to be able to be categorised (Gale *et al.*, 2013).

Framework analysis was developed in the 1980s for large-scale policy research by Jane Ritchie and Liz Spencer (Gale *et al.*, 2013, Smith and Firth, 2011). It is not aligned with a particular philosophical, theoretical or epistemological approach (but adheres closely ontologically to subtle realism) and borrows principles from different epistemological traditions (Ward *et al.*, 2013, Gale *et al.*, 2013). It is a type of thematic analysis but goes beyond thematic analysis as it looks at relationships between codes (mapping and interpretation) (Green and Thorogood, 2009).

Unlike entirely inductive approaches, such as grounded theory, with framework analysis an *a priori* approach can be taken (Pope *et al.*, 2000, Smith and Firth, 2011) and analysis and can sit anywhere along the inductive-deductive continuum (Gale *et al.*, 2013). Using framework analysis, specific predefined themes can be explored but unexpected findings and other aspects of participants' experiences can also be discovered and analysed (Srivastava and Thomson, 2009). Data collection can either occur before analysis or analysis can start during the data collection process (Srivastava and Thomson, 2009, Ward *et al.*, 2013).

Framework analysis emphasises transparency in data analysis and maintains an effective and transparent audit trail enhancing the rigour and credibility of findings (Smith and Firth, 2011). It follows specific steps; familiarisation, identifying a thematic framework, indexing, charting, mapping and interpretation (table 5.1). The first four steps are mainly data management strategies with the bulk of the interpretation taking place

during the mapping phase (Ritchie and Spencer, 1994). The defining feature of framework analysis is the matrix output containing rows (cases), columns (codes) and cells of summarised data, which provides a structure to systematically reduce data and analyse it code by code (Gale *et al.*, 2013).

Summary of the pragmatic qualitative research approach

- Pragmatic qualitative research aligned with the project's overarching philosophical paradigm, pragmatism.
- A qualitative descriptive study, a type of pragmatic qualitative research, was used in this study.
- Qualitative descriptive studies collect data through interviews or focus groups. Interviews tend to be semi-structured or unstructured.
- Purposive sampling is recommended.
- An inductive approach is taken to data analysis and qualitative content analysis can be used. Framework analysis was used in this study.

Table 5.1 Steps taken during framework analysis

Steps taken during framework analysis	Definition
Familiarisation	The researcher becomes immersed in and familiar with the data through listening to tapes and reading transcripts (Pope *et al.*, 2000, Srivastava and Thomson, 2009).
Identifying a thematic / analytical framework	A thematic / analytical framework, a set of codes organised into categories (Gale *et al.*, 2013) is developed to provide a mechanism for labelling and managing data for subsequent retrieval and exploration (Ritchie and Spencer, 1994).
Indexing	Indexing refers to the stage when the thematic / analytical framework is applied to the coded data (Ritchie and Spencer, 1994).
Charting	Summarised data are entered into a framework method matrix which is a spreadsheet with codes in columns and cases in rows (field notes can be included in the matrix) (Gale *et al.*, 2013). Charting can be thematic and look at one theme across all respondents or by case and look at each response across all themes (Ritchie and Spencer, 1994). Data should always be clearly identified as to where it came from (Srivastava and Thomson, 2009) and Ward *et al.* (2013) advises indicating particularly rich or meaningful quotations.
Mapping and interpretation.	Charts can be interpreted through analytic memos, typologies identified and connections between categories explored (Gale *et al.*, 2013). The range and nature of the phenomena can be mapped, concepts defined, explanations provided and strategies developed (Ritchie and Spencer, 1994).
Additional stage which can be undertaken after charting (not included specifically in framework analysis)	
Descriptive analysis	Descriptive analysis was not included in Ritchie and Spencer, (1994) framework analysis but has been recommended subsequently by Ritchie *et al.*, (2003b). It involves detection, categorisation and classification of data in each column (code) of the charted data to understand what is happening within a single subtopic. Detection involves noting the range of perceptions, views and experiences or behaviours. Elements, definitions and constructs can then be identified. Once this is done data can be classified and grouped under higher order labels. During the first stage of abstraction descriptions stay close to the original data, but later the data becomes interpreted in a more conceptual way (Ritchie *et al.*, 2003b).

5.5 Methods

The study was informed and built on existing knowledge and ideas developed during the literature review (Chapter 2). Existing data were explored prior to data collection to ensure a good sense of the substantive issues of the research topic, ensure clarity about what could be built upon and know what had been generated previously. The study aimed to allow for inquiry to be carried out in a way that would expose the views of those involved, allow for critique, and provide opportunity for revised or new themes to emerge.

The research was carried out under the pragmatic paradigm using pragmatic qualitative research methodology and a qualitative descriptive study design. It was as emergent as it could be given the fact that a literature review had already been undertaken, a protocol designed and the interview topic guide had been developed through these prior assumptions. The researcher remained reflexive throughout the data gathering and data analysis stages. The topic guide was developed *a priori* but was emergent and developed throughout the study, interviews were semi-structured and allowed for the emergence of new themes, transcripts were predominately open coded and allowed for the emergence of new categories. The researcher's personal and intuitive knowledge guided the inquiry process and during the study the researcher worked inductively and remained open to new concepts and themes. Although data collection was not done in conjunction with data analysis (indexing, charting, mapping) past interviews influenced future ones in that themes identified during familiarisation and coding were explored during subsequent interviews.

5.5.1 Recruitment process and study sample

Potential participants were initially identified and informed of the study by a physiotherapist working at the ARU. Participants who expressed interest were then approached by the researcher, provided with verbal and written information about the study (appendix 5.2) and advised to take up to 7 days to read and reflect on the information provided and consider whether they wished to take part in the study. No consent was obtained at the time of recruitment and all participants were advised to take a minimum of 24 hours before consenting to participate. If there were any

questions or concerns about the study the researcher was available for discussion. Before commencement of the interview, two signed consent forms (one for participant and one for researcher) were obtained from participants (appendix 5.3). Participants who wished to withdraw after providing informed consent were withdrawn and their data not used.

Inclusion criteria for the study included; (1) inpatient at ARU at time of interview, (2) male or female, (3) 18 years or above, (4) lower limb amputation (greater than a toe), (5) current or past experience of PLSd, (5) full cognitive ability, (6) able to communicate in English. Exclusion criteria; (1) other severe health complications.

In keeping with pragmatic qualitative research methodology, the non-probability sampling maximum variation purposive sampling was used to identify information-rich cases (Savin-Baden and Howell Major, 2013). This was used to ensure that key areas relevant to the subject matter were covered but some diversity of participant characteristics were included. To achieve a sample that was inclusive of the demographic structure of the population being studied, as recommended by Ritchie *et al.* (2003a), an *a priori* sample quota was developed. Reason for amputation, age and gender were all used in the body of the quota to capture diversity, ensure rich and deep data and to ensure variations across the sample. Table 5.2 provides details of the quota of male and female participants of different age and reason for amputation which the study aimed to include.

Table 5.2 Qualitative descriptive study sample quota

Sample Quota			
	Vascular Amputation	Trauma / disease / infection causing eventual amputation	Trauma / disease / infection causing immediate amputation
Males:			
≤65 years	1-4	1-3	1-2
>65 years	1-4	1-3	
Females			
≤65 years	1-4	1-3	0-2
>65 years	1-4	1-3	

Sample size is dependent on the theoretical underpinning and methodology of the study, the breath and scope of the research question, the social population being investigated and their heterogeneity and the time and resources available. Data collection should stop once data saturation has been reached (Baker and Edwards, 2012). Due to these many considerations, sample size varies widely in qualitative research (1-95 sample size across doctoral thesis in Great Britain and Ireland (Baker and Edwards, 2012)). Taking these points into consideration and through review of past qualitative papers on the acceptability of acupuncture (Hopton *et al.*, 2013, Schapira *et al.*, 2014), the experience of amputation (Murray and Forshaw, 2013) and the experience of PLSd (section 2.5), a sample size of 15 participants was set *a priori* and in line with qualitative descriptive studies was deemed adequate. Data saturation was anticipated to occur within this number of interviews. Had data saturation not been achieved, depending on the time taken to recruit 15 participants, the researcher would have considered approaching the ethical board approving this study to ask for amendments to the study protocol.

5.5.2 Data collection

Taking into account the research question and the study design, semi-structured interviews were used to collect data. One to one interviews were chosen over focus groups as interviews provide an opportunity for detailed investigation of each participant's personal perspective and allow understanding of personal context and complex issues, whereas focus groups offer less opportunity for the detailed generation of individual accounts (Lewis, 2003). Also, practically, focus groups would have been difficult to implement due to the requirement of having to recruit several participants within a set timeframe as participants were only inpatients at the ARU for up to 7 weeks.

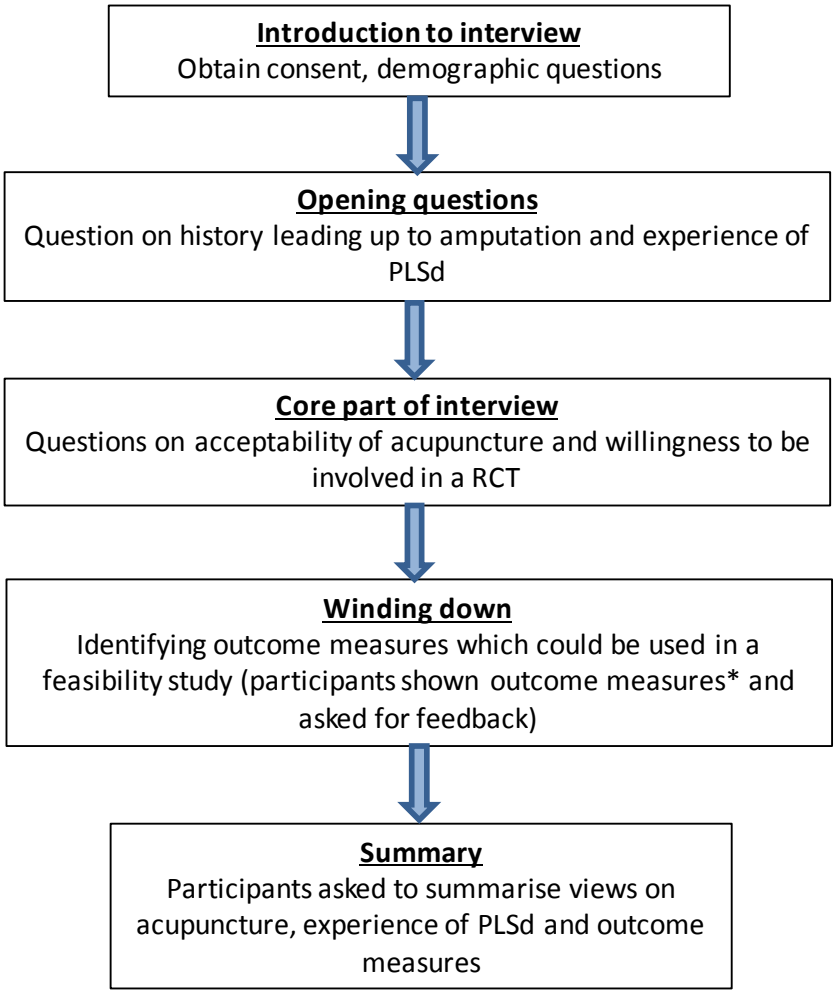
Participants were interviewed in their natural settings (at the ARU, whilst the participants were inpatients) at a time convenient to the participant in a room where only the researcher and the participant were present. All interviews followed a topic guide (appendix 5.4), were audio-recorded, facilitated by the researcher, lasted for approximately one hour (between 45 minutes to 1½ hours) and were transcribed verbatim. As a process of error reduction and to enhance credibility, respondent validation was obtained post transcription of interviews. Participants were interviewed

once only and no repeat interviews were carried out. The topic guide was developed through review of relevant literature, through discussion with other members of the research team and was modified during the interview process to allow for the capturing of new themes.

The interviews were semi-structured and flexible, allowing the interviewer to alter the sequence of questions and the way in which they were phrased (Arthur and Nazroo, 2003). This approach was taken with the intent of producing rich, detailed data. Interviews were informal, allowing the participant to direct the interview in any direction, but the topic guide was always returned to and the researcher played an active role in moving the discussion through specific areas.

The interviews were conducted as recommended by Arthur and Nazroo (2003) (figure 5.2). All interviews commenced with opening unthreatening topics, asking participants about their demographics. This was followed by asking participants to recount their history of events leading up to the amputation, and acceptability of acupuncture. This naturally allowed participants to describe their experience of living with PLSd within the interview. All participants were asked about any past experience of acupuncture and their perceived acceptability of acupuncture for treating PLSd. Participants were also shown a range of outcome measures with the last five participants completing all of them. Participants were invited to give feedback on how they found completing these outcomes and any preferences they had. Outcome measures shown to participants are listed in figure 5.2. These were chosen from the recommendations from the Assessment Committee of the Neuropathic Pain Special Interest Group (NeuPSIG) and from recommendations from the Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials (IMPACT-II) as described in section 6.5.4. At the end of the interview, to help highlight views and ensure the researcher left with a complete/accurate picture of the participant's views, questions were asked seeking an overall summary of participants' perceived acceptability of acupuncture, willingness to be involved in a RCT and attitudes and experiences of PLSd.

Figure 5.2 Structure of semi-structured interviews



**Outcome measures: Short Form McGill Pain Questionnaire 2 (SF-MPQ-2), Neuropathic pain symptom inventory (NPSI), Neuropathic pain scale (NPS), Numerical Rating Scale (NRS), EuroQol-5 Dimensions (EQ-5D-5L), Brief Pain Inventory (BPI), Insomnia Severity Index (ISI), Hospital Anxiety and Depression Scale (HADS), Perceived Stress Scale (PSS), Patient Global Impression of Change (PGIC).*

Social differences did exist between the researcher and the participants in relation to age, gender, nationality, race and socio-economic status and the researcher used her past clinical experience of dealing with diverse patient groups to help counteract this. However, it was noted that this may have influenced rapport and the interview data produced. Green and Thorogood (2009) state that building a sense of trust involves the interviewer being both non-judgmental and interested. The researcher avoided questions and expressions that suggested disagreement or disapproval and aimed to have a genuine and respectful interest in the participant. The researcher aimed to understand the participant's perspectives, listen to the account of the participant,

encourage the participant to continue and make the participant feel safe to reveal their views. It was noted that working with one's own language does not eradicate problems of translation. Shared meanings may be assumed, but in reality different cultural groups may use particular terms in different ways (Green and Thorogood, 2009). The researcher aimed to avoid interruption and disruption of the flow of the interview but requested clarification of a point when required. The researcher aimed to avoid: technical and professional vocabulary, leading questions which implied a preferred answer, judgment and closed questions.

The researcher was aware of her influence on data collection and analysis (section 5.8) and kept field notes and a brief reflexive journal to provide self-awareness on her influence on data collection / analysis. Field notes were made during and immediately after the interview and enabled the researcher to record thoughts and issues that may be relevant during analysis (Ward *et al.*, 2013). A reflexive journal was kept to ensure procedures and emerging ideas were recorded and to improve trustworthiness, as credibility is increased when the researcher describes and interprets their experience (Koch, 2006).

5.5.3 Data analysis

In keeping with pragmatic qualitative research and qualitative descriptive studies, analysis aimed to summarise the data, presenting the facts, feelings and experience of the participants (Sandelowski, 2000 and Savin-Baden and Howell Major 2013). Analysis aimed to capture the substantive meaning of the data. Although data collection was not done in conjunction with data analysis the researcher became familiar with and coded and re-coded the transcripts during the data collection phase. Indexing, charting and interpretation were done only post completion of data collection.

Within 24 hours of the interview the researcher listened to the recording of the interview and completed field notes. The audio-recorded interviews were transcribed verbatim. The computer qualitative data analysis software program NVIVO 10 was used to develop the theoretical / analytical framework and index transcripts. This provided the advantage of the whole transcript being easily accessible, enabling the researcher to easily and instantaneously be able to refer back to the whole transcript, ensuring the

context of the data were not lost**.** Charting can be devised on MS word or using a MS Excel spreadsheet (Fuber, 2010). Excel is recommended by Swallow *et al.* (2003) and was used in this study as described below. Excel was also used for descriptive analysis of data. Data collection aimed to be transparent, comparative and reflexive. To ensure transparency the researcher tried to be explicit about the steps taken during data production and analysis. Stages undertaken during data analysis followed Ritchie and Spencer (1994) guidelines and included:

Transcription: Interruptions and non-verbal communication were bracketed and noted within the text. Unclear speech was noted with question marks. All transcripts were checked for errors by listening to the audio-recording and reading the transcripts simultaneously.

Familiarisation: The researcher became immersed in the data and became familiar with the data through listening to tapes and reading transcripts and identified initial themes and categories. As advised by Ritchie and Spencer (1994) the researcher listed key ideas and recurrent themes during this stage of analysis and the general atmosphere within the interview when exploring difficult topics.

Coding: Paraphrases and labels were used to code what had been interpreted in the transcript. Notes were also made in the margins of the transcript of the main ideas appearing in the data (Fuber, 2010). In this study as the research was neither completely inductive or deductive, both a mixture of open coding and predefined coding was used. Coding was thematic and could range from only a few words, to part of a sentence to whole paragraphs.

Identifying a thematic / analytical framework: Drawing on both the interview topic guide and emergent issues raised by the participants, categories were developed both inductively and deductively from the data. A miscellaneous code was included under each category to avoid ignoring data that did not fit the analytical framework (Gale *et al.*, 2013). The analytical framework was refined over time and as found by Ritchie and Spencer (1994), although the first version of the thematic / analytical framework was largely rooted in *a priori* issues, it became more responsive to emergent and analytical themes over time.

Indexing: The thematic framework was applied systematically to all data. As advised by Pope *et al.* (2000) data were kept in textual form. Ritchie and Spencer (1994) state that indexing involves making judgments about the significance and meaning of data and single passages often contain a number of different themes each of which need to be referenced, and this was found to be the case in this study. Passages which contained references to more than one category were multi indexed as advised by Ritchie *et al.* (2003b).

Charting: Analysis was thematic with charts drawn up as recommended by Ritchie and Spencer (1994) for each key subject area, and entries made for all respondents on each chart. As advised by Ritchie and Spencer (1994) cases were always kept in the same order so that the whole data set for each case could be easily reviewed. All data were clearly referenced so the researcher could always go back to the original data and particularly meaningful quotes were included verbatim in the charts in blue italics. As recommended by Fuber (2010) all data were included in charting, even if it did not initially appear relevant to the study. In keeping with recommendations from Ritchie *et al.* (2003b) the first column of each chart was reserved for case identification and main demographic details were also included here. Each column was assigned a number to ensure easy reference between columns and a column was reserved for the researcher's comments to facilitate interpretative observations throughout the analysis process. As much as possible, words used by the respondents were used during charting (figure. 5.3).

Descriptive analysis, mapping and Interpretation: When all the data had been charted, the data set was interpreted as a whole. As advised by Ritchie *et al.* (2003b) to gain understanding of what was happening within a single subtopic, within each column (code) data were detected, categorised and classified (figure 5.4). Analytic memos were used to aid mapping and interpretation.

Figure 5.3 Example of charted data

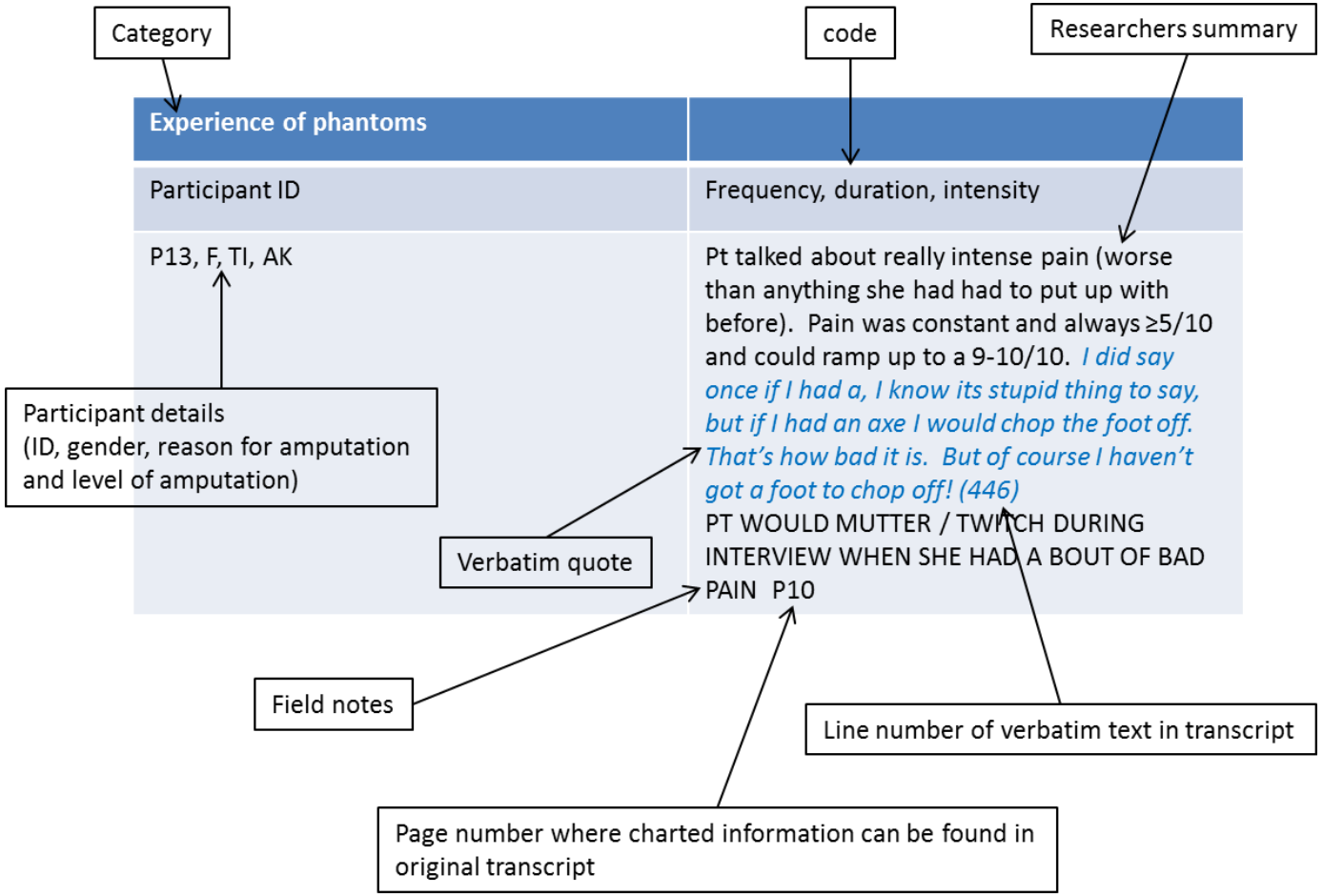
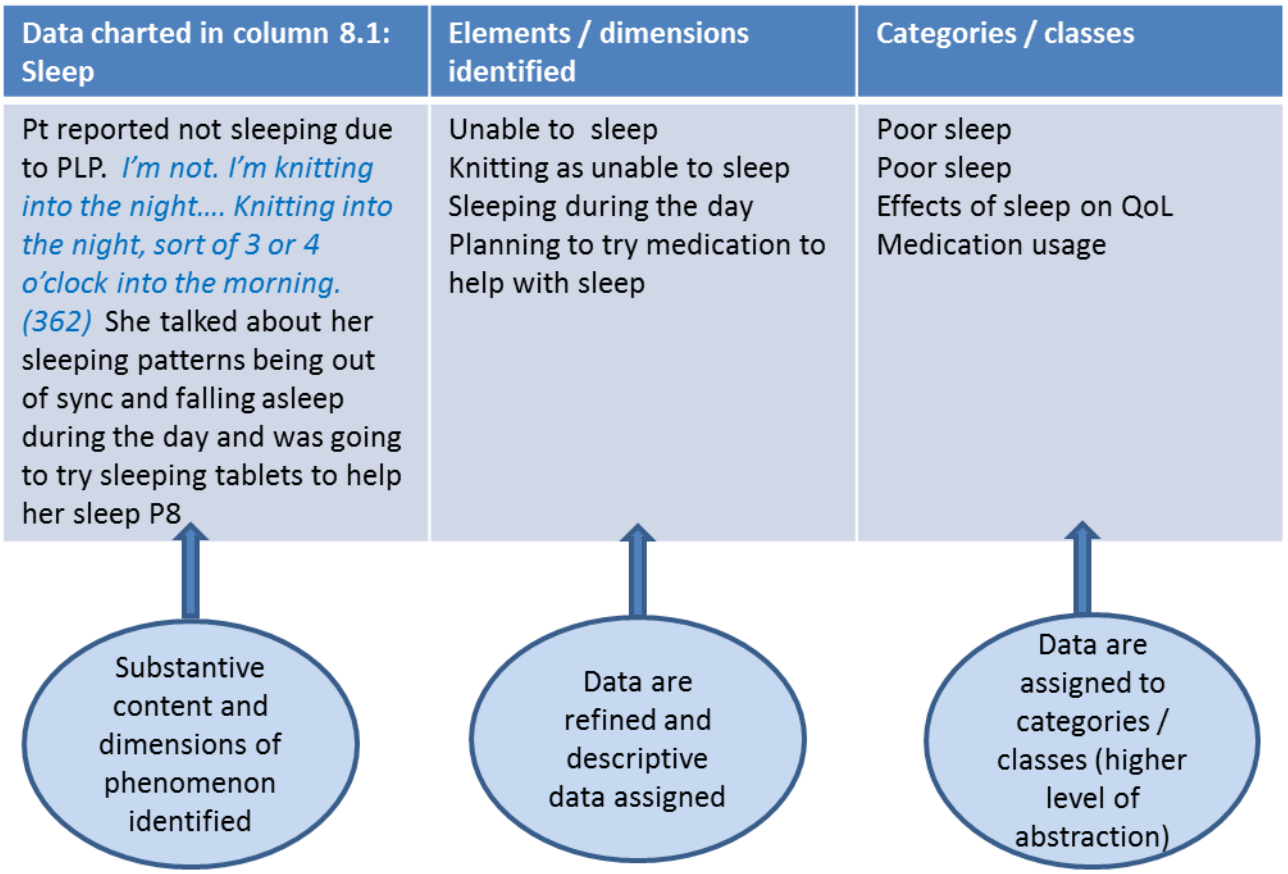


Figure 5.4 Example of descriptive analysis



Peer debriefing took place throughout the research process. The researcher met with two peers who questioned methods, data analysis, emerging conclusions and biases. One independent researcher checked the pathways of decisions made during data analysis. Two researchers (the author and one other) separately coded three transcripts and the results were compared and discussed. A code-recode procedure was also adopted where the author recoded a segment of data two weeks after initial coding and results were compared. Two researchers (the author and one other) independently coded and indexed a transcript using the analytical framework. This was done to ensure credibility and dependability of findings.

5.5.4 Ensuring rigor in qualitative data analysis

Qualitative research rejects a naïve realist ontological position, holding that the criteria reliability, validity and generalisability cannot be used to judge quality (Mays and Pope, 2000). The quality of qualitative research has been considered in a variety of alternative ways including; trustworthiness, authenticity, goodness, relevance and plausibility (Savin-Baden and Howell Major, 2013). The gold standard criteria related to qualitative research is Lincoln and Guba's (1985) trustworthiness criteria; credibility, transferability, dependability and confirmability (Savin-Baden and Howell Major, 2013) and this was used in this study.

5.5.4.1 Credibility

Credibility can be ensured through using appropriate research methods (Shenton, 2004). The study tried to be explicit about the underlying philosophical and methodological standing of the research to justify methods used. The researcher tried to ensure there was congruence between the research question, methods and analytical processes used (Savin-Baden and Howell Major, 2013). Results tried to provide thick description / in depth illustration to aid credibility (Tracy, 2010).

Prolonged engagement increases exposure of the researcher to the researched (Savin-Baden and Howell Major, 2013) but in this study the researcher was unable to spend extensive periods of time at the ARU making herself a 'member of the group' and absorbing the context of the study. Although it could be argued that this lack of

prolonged time spent in the field may have prevented a relationship of trust (Shenton, 2004) and access to tacit knowledge (Tracy, 2010) it could also be argued that being an independent researcher outside of participants' clinical care may have been advantageous, in that sometimes people are more willing to disclose information to strangers (Shenton, 2004). Additionally prolonged engagement risks causing researchers to become so immersed in the study that their professional judgement may be influenced (Lincoln and Guba, 1985).

The researcher was aware that transparency and honesty were needed about any biases and goals and the impact she had on participants (Tracy, 2010). She was aware that her *a priori* knowledge and values may distort findings (Savin-Baden and Howell Major, 2013). The researcher aimed to make her position clear to allow the reader to determine whether bias unnecessarily influenced results and provided a reflexive commentary on her influence on the study. The researcher was aware that despite not disclosing her professional background as an acupuncturist and physiotherapist, participants may have distorted the data through wanting to please, say appropriate things or through not being motivated during the interview (Lincoln and Guba, 1985). However, she tried to ensure honesty by encouraging participants to be frank and through iterative questioning (Shenton, 2004).

Triangulation can aid credibility through providing multiple data points that broaden the understanding of the subject under research (Savin-Baden and Howell Major, 2013). Findings are more credible when different sources of data converge on the same conclusions (Tracy, 2010). Different types of triangulation exist including data, investigator, theory, methodological and environmental (Guion, 2002). Due to this study being one stage of an overall project, triangulation was not undertaken. It is acknowledged that this may make results less credible.

Member checking involves verification of interpretation with participants (Savin-Baden and Howell Major, 2013). In this study data were not formally member checked as ethically participants are often not consciously aware of information found by the researcher and can become upset by it (Krefting, 1991). Also, participants may have changed their viewpoint from time of data collection (Appleton and King, 1997). However, during the interviews informal member checking (the researcher summarising

what had been said) did take place to ensure meaning was not lost. Respondent validation provides credibility to the research (Mays and Pope, 2000). As a process of error reduction and to enhance credibility, respondent validation was obtained post transcription of interviews.

Negative case analysis requires identifying data that do not support emerging themes, with the aim of refining analysis until it explains the majority of cases (Savin-Baden and Howell Major, 2013). The charting process of framework analysis ensured all data were included and addressed during analysis.

Peer debriefing took place throughout the research process. The researcher met with colleagues who questioned methods, data analysis, emerging conclusions and biases. Although these colleagues were the researcher's seniors, there were good relationships, debriefing was empathic and discussion was not judged. Peer debriefing ensured the research was honest, that the researcher's biases were probed and interpretations were clarified (Shenton, 2004).

In qualitative studies, data collection should continue until saturation has been met. In this study, as it had a fixed sample size, it risked being completed before reaching data saturation. The researcher asked herself the questions 'are there enough data to support significant claims?' and 'was enough time spent gathering interesting and significant data?' (Tracy, 2010). Overall, the researcher felt that she could answer yes to these questions and felt that data saturation had been met as during the final interviews no new codes or categories emerged.

5.5.4.2 Transferability

The researcher viewed transferability as the responsibility of the reader (Krefting, 1991). To aid transferability, information was provided on the context of the research, the inclusion / exclusion criteria of participants, the number of participants involved, data collection methods employed, the number and length of interviews and the time period over which the data were collected (Shenton, 2004). A dense description of methods was provided (Savin-Baden and Howell Major, 2013). Purposive sampling provides stringent conditions and maximises the range of information collected (Ritchie *et al.*,

2003a) and through this method the researcher tried to recruit a range of participants. However, it was noted that no female vascular amputees of ≤65 years were identified or recruited and therefore the sampling quota was not met. This may make the findings less transferable to other settings.

5.5.4.3 Dependability

Dependability can be achieved through reporting in detail the processes involved in a study (Shenton, 2004) ensuring the research process is logical, traceable and clearly documented (Tobin and Begley, 2004). To ensure dependability a dense description of research methods was recorded and the researcher aimed to be consistent throughout the study. Through using framework analysis, taking field notes and memos, the researcher ensured the data were auditable. Additionally two researchers coded three transcripts, two researchers coded and indexed one transcript and the researcher used a code-recode procedure to ensure dependability.

5.5.4.4 Confirmability

Confirmability ensures interpretations of findings are clearly derived from the data and is ensured when credibility, transferability and dependability is achieved (Koch, 2006, Tobin and Begley, 2004). It is a term which suggests the researcher has remained neutral during data analysis and interpretation (Savin-Baden and Howell Major, 2013) and findings are the results of the experiences of participants, not the preferences of the researcher (Shenton, 2004). Confirmability can be ensured through the researcher acknowledging their own predispositions and through providing a clear audit trail, allowing others to view procedures and decisions made (Shenton, 2004). In this study the researcher acknowledged her predispositions and data produced was auditable. Raw data (the transcripts) were stored. Field notes were kept. NVIVO 10 enabled coding and indexing to be transparent and charting and descriptive analysis is in itself a transparent way of data reconstruction. Memos / progress notes were kept as was a brief reflexive journal.

5.5.5 Ethics

NRES Committee London - Brent and Guy's and St Thomas' R&D granted ethical approval

for this study respectively on 6.11.2013 and 29.11.2013. London South Bank University granted ethical approval on 21.11.2013 (appendix 5.5). The study commenced in December 2013 and data collection was completed in June 2014.

The study was designed to develop new knowledge, and had realistic and achievable objectives (Savin-Baden and Howell Major, 2013). All participants were provided with clear information about the purpose of the study, how the data would be used and what was required of them (Lewis, 2003). To ensure participants had time to reflect on both verbal information and the participant information sheet before volunteering, no participants were recruited until at least 24 hours post initial contact with the researcher. The participant information sheet was considered to provide adequate information and be presented in plain language. It informed on expectations, risks, data management and contact details of the researcher (Savin-Baden and Howell Major, 2013). Signed consent was always obtained before recruiting a participant into the study. All participation was voluntary and participants were free to withdraw from the study at any time without compromising their standard of care. Participants were given the researcher's contact details (phone and email) to ensure they were able to contact the researcher and withdraw if required.

As qualitative data can produce personal and identifiable data (Mason, 2002) care was taken to ensure confidentiality and anonymity. The researcher was aware of her role to ensure participants' privacy and confidentiality (Savin-Baden and Howell Major, 2013). Identifiers from interviews were removed from transcripts and all data labelled with a participant identification number only. Identifying information was stored separately from other data. Demographic data provided in reports and publications was not detailed enough to allow for participant identification. All members of the research team treated all data confidentially and no information was disclosed outside of the research setting. Transcripts were kept in a locked filing cabinet and on a password protected computer. A master list of the participants' names and identification was developed and kept in a separately locked filing cabinet, away from other data. All hard copies of data were stored at London South Bank University.

The potential for benefit was considered to outweigh the potential for harm from the study (Savin-Baden and Howell Major, 2013). No risk of potential physical harm was

identified. Through prior discussion with physiotherapists and doctors at the ARU, it was not anticipated that the interviews would be psychologically harmful or distressing to participants. All interviews were conducted with autonomy (respect the rights of the individual), beneficence (doing good) and non - maleficence (do no harm). Interviews were carried out with regard for the participant as an individual and all views were respected. The researcher aimed to carry out interviews with empathy and understanding, giving participants time to talk about their concerns and reflect on their experiences. The researcher tried to be alert to signs of discomfort and unwillingness of the participant to continue, and participants were provided with real opportunities to refuse questions or withdraw from the interview / study both throughout and after the interview process. To offset any power imbalance between the researcher and the participant, the interview aimed to be conducted in a friendly open manner. No vulnerable adults were enrolled into the study (Savin-Baden and Howell Major, 2013).

The researcher maintained her role as a researcher and not a clinician and did not offer advice to participants. When asked for advice, she recommended participants spoke to clinical staff at the ARU. If any information emerged which suggested participants were at risk of harm, the researcher planned to encourage participants to report this themselves, or gain consent from the participant to report it for them.

The researcher was at minimal risk during fieldwork. All interviews were conducted at the ARU and clinical staff were always available. Other researchers were aware of her whereabouts.

5.5.6 Conventions used when writing up results

In keeping with the qualitative descriptive design used in this study, numerical data on frequencies were provided in results (Sandelowski, 2000). Qualitative research sometimes rejects the use of numerical data in studies for philosophical reasons and it could be argued that numerical data are incompatible with qualitative research (Maxwell, 2010). However, numbers are integral to qualitative data and the meaning qualitative researchers seek depends in part on numbers. Counting is part of the analysis process especially for recognising patterns and deviation from patterns (Sandelowski, 2001). Qualitative researchers frequently make quantitative claims using

terms such as 'many', 'often' and 'sometimes' but providing numbers make these claims more precise (Maxwell, 2010). Providing quantitative data ensures evidence is adequately presented and helps counter claims that evidence has been cherry-picked (Maxwell, 2010). Therefore, although it is recognised that numerical data can lead to inference of greater generality than is justified, and the use of numbers can lead to a slide into a variance way of thinking (Maxwell, 2010), numbers were used in the results.

In the results section, when presenting verbatim quotes, conventions were used as detailed in figure 5.5.

Figure 5.5 Presentation of quotes in qualitative descriptive study

Conventions used when presenting quotes in results

- Participants were each given an identification number (P1-P17).
- Gender M/F and nature of amputation T/I/V/U were recorded.
- Square brackets [ ] contained information added to provide meaning and content to the quote.
- Dots…. indicated data taken out of the quote to keep the quote succinct.
- ??? indicated unclear speech.

Key: M, male; F, female; T, trauma; I, infection; V, vascular; U, ulcer.

Summary of qualitative descriptive study methods

- The study was undertaken at an ARU in London.
- The qualitative study was situated under the project's overarching philosophical stance of pragmatism. A pragmatic qualitative research methodology and qualitative cross-sectional descriptive study design was used. Data were collected through semi-structured interviews.
- The study aimed to recruit 15 lower limb amputees with past or current experience of PLSd and collect data on the acceptability of acupuncture, willingness to be involved in a RCT, experience of PLSd and identify appropriate outcome measures which could be used in a feasibility study.
- Data were analysed using framework analysis.

5.6 Results

A total of 17 lower limb amputees were approached about the study. Of these 16 agreed to participate and were interviewed. One dropped out after interview and requested for their data not to be used. Additionally one interview was terminated early and the participant was not questioned about acceptability of acupuncture (due to participant fatigue). The participant did not wish to continue the interview at another time. Figure 5.6 shows participant flow through the study.

Demographics of participants (n=15) included in the study are shown in Table 5.3. The majority of participants were white British (n=11), male (n=12), and had not undergone previous amputations (n=14). Participants had undergone below knee (n=8), above knee (n=6) and through knee (n=1) amputations due to vascular disorders (n=8) or trauma (+/- associated infection) (n=7). Only two participants underwent immediate amputation due to trauma. Throughout the duration of the study no female's ≤ 65 years were identified who had an amputation due to vascular pathology. Therefore the sample quota was not fully achieved.

Key themes and sub-themes identified during data analysis are presented in figure 5.7. Themes are presented by relevance to the overall project, and as the main objective of this study was to explore amputees' perception of the acceptability of acupuncture, this theme was described first. However, during the interviews it emerged that this was not the most important theme for participants. Theme 1 describes participants' understanding and perceived acceptability of acupuncture, theme 2-3 amputees' experience of undergoing an amputation and theme 4-6 the experience of living with PLSd. Theme 7 provides feedback on outcome measures.

Figure 5.6 Participant flow through the qualitative descriptive study

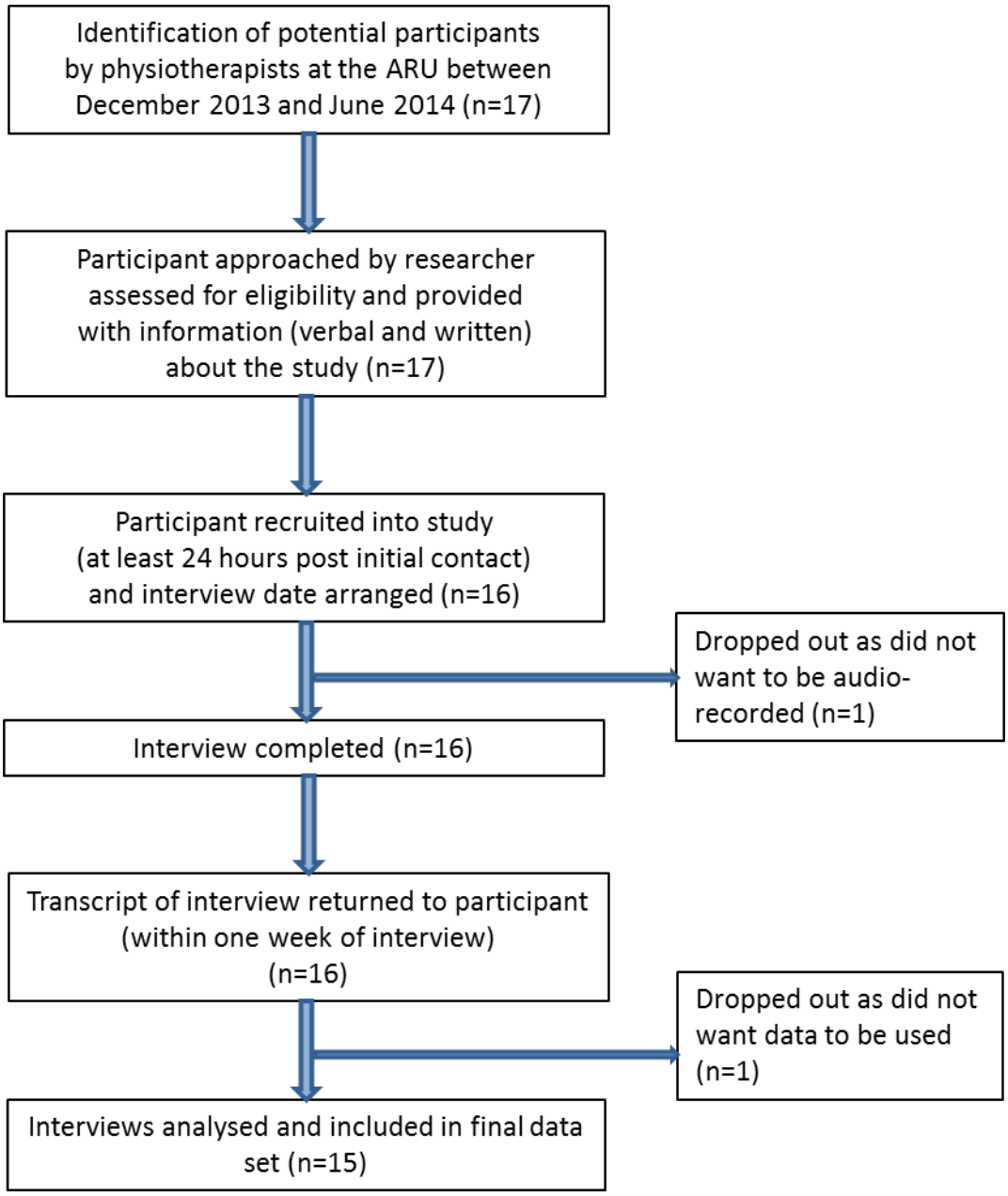
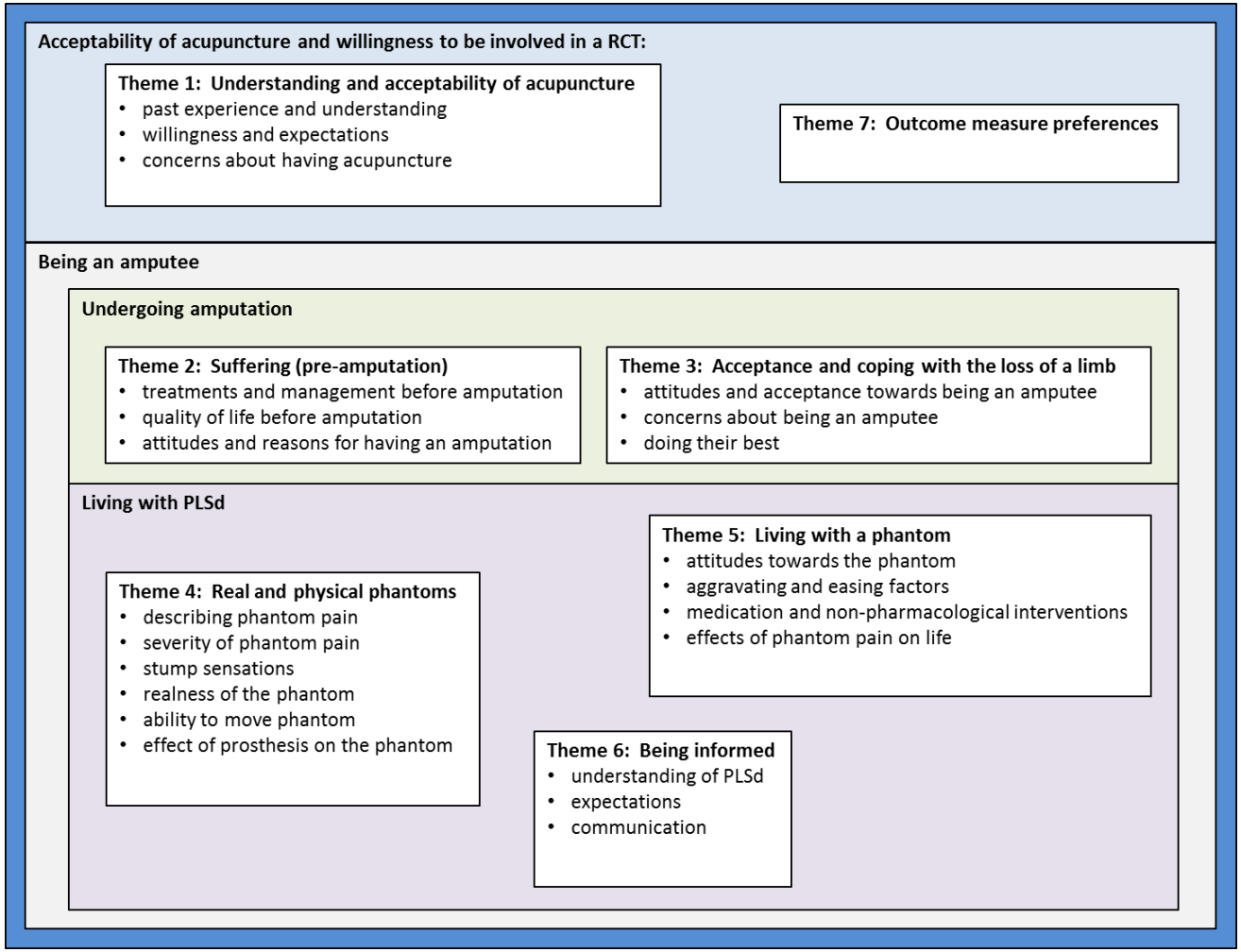


Table 5.3 Qualitative descriptive study, participant demographics

Participant ID	Age	Gender	Ethnicity	Employment status	Diabetes	Amputation level	Time since amputation	Reason for amputation	Previous amputations	Past experience of acupuncture
1	54	Male	White British	NW (2012)	Yes (Type II)	BK	2m	V/U	No	No
2	58	Male	Black British	NW (2010)	No	AK	2m	V	No	Yes
3	84	Female	White British	R	No	BK	2m	V/U	No	Yes
6	75	Male	White British	R	Yes (Type II)	AK	3m	V	No	No
7	26	Male	White British	W	No	BK	1m	T	No	Yes
8	62	Male	White British	W	No	AK	1m	T/I	No	Yes
9	66	Male	White Irish	R	Yes (Type II)	AK	1m	V	No	No
10	60	Male	White British	UE	No	AK	1m	T/I	No	Yes
11	67	Male	White British	R	No	TK	1m	V/U	No	Yes
12	35	Male	White Other	W	No	BK	3m	T	No	No
13	54	Female	White British	NW (2009)	No	AK	1m	T/I	No	No
14	66	Male	Mixed Caribean	R	Yes (Type II)	BK	1m	T/I	No	Yes
15	45	Male	White British	W	No	BK	1m	V/U	No	No
16	82	Female	White British	R	No	BK	1m	T/I	No	N/A
17	35	Male	White British	W	Yes (Type I)	BK	1m	V/U	Yes (toes and part of foot)	No

Key: NW, not working (date last worked); R, retired; W, working; UE, unemployed;
BK, below knee; AK, above knee; TK, knee disarticulation; V, vascular; U, ulcer; T, trauma; I, infection; N/A, not asked; m, month.

Figure 5.7 Qualitative descriptive study, key themes and sub-themes



5.6.1 Theme 1: Understanding and acceptability of acupuncture

This theme describes participants' understanding of acupuncture, perceived acceptability of this intervention, willingness to be involved in a RCT and expectations of benefit from treatment.

Subtheme: past experience and understanding: Half of the participants had no prior experience of acupuncture (table.5.3). Those that had experienced acupuncture had done so for a variety of reasons including; addiction, low back pain, stress, neuropathic pain, and rheumatoid arthritis. Past reported benefits of acupuncture ranged from having resolved symptoms, given short term benefit and not been beneficial. Several of those who had past experience of acupuncture found it painful or did not enjoy it and one participant felt that his mood affected the effectiveness of treatment. Participants generally had a basic understanding of what acupuncture was. Two participants felt there needed to be a belief in acupuncture for it to work.

> *"I think it's good. I feel I've got, it's helped me with psychological and physical things and both, when I've used it for different things both times it's been effective."(P7,M,T)*

> *"It's alright for some people who have the imagination… and you stick needles in or give them a drink of water and they think, oh I'm cured… cured, because it's all imagination with them…. With acupuncture you stick needles in and you think oh I'm cured he stuck needles into me"(P9,M,V)*

Subtheme: willingness and expectations: Participants were generally willing to try acupuncture for PLSd and be included in a RCT with only two male participants not considering it. Reasons for trying acupuncture included being prepared to try anything, that there was a need to experiment with different treatment techniques and remain open-minded to different interventions. One participant was willing to try acupuncture as it may help others even if not himself. Participants who had not had positive past experiences of acupuncture were generally still willing to try it for PLSd.

> *"You could stick pins up my backside if it would stop the bloody pain!... if it got rid of it I would be willing to try anything"(P8,M,TI)*

One participant was only willing to have acupuncture if he felt the practitioner was properly qualified. Two participants felt either PLSd was not severe enough to warrant acupuncture or that symptoms were improving so didn't want to try acupuncture at that time. Both were willing to try acupuncture if symptoms worsened or did not resolve. The two who were not willing to try acupuncture either didn't believe in acupuncture and were worried it would aggravate symptoms or had not had positive past experiences (painful and providing short term relief only).

> *"I don't know, I just didn't enjoy it last time. And I think I won't enjoy it this time. That's what makes me feel it's no good for me."(P11,M,VU)*

Participants were willing to have acupuncture on average twice weekly. Younger participants were generally happy to have acupuncture more frequently and even daily as long as it didn't clash with other hospital appointments, whereas older participants expressed a need for time to rest. One participant felt that if acupuncture was beneficial he would be willing to have acupuncture more frequently than if it was not. Whilst at the ARU participants generally felt they had time for acupuncture and there was an attitude of may as well have acupuncture as 'I'm not doing anything else am I'. Fitting several acupuncture treatments into the weekly schedule was considered feasible.

> *"Well I suppose you could do it every day cause you've got time, but sometimes doing physio and OT you are knackered afterwards…. So to think to yourself one o'clock you've got OT, two o'clock you've got physio and then half past three you've got acupuncture. I wouldn't like that, I would think no it's too much"(P11,M,VU)*

> *"you've got hours and hours of just wasted time. Um, so while you are upstairs really there's no reason why you couldn't do a session a day, because it's so much wasted time here"(P15,M,VU)*

Participants generally expected to experience a reduction in pain and experience some effects of acupuncture within a couple of weeks of starting treatment. Participants generally talked about trying acupuncture for a couple of weeks or approximately five or six sessions. One participant talked about continuing treatment as long as necessary

and another did not know what to expect.

> *"I think after two weeks I would get a good idea whether it's worth doing in the long term"(P7,M,T)*

Subtheme: concerns about having acupuncture: Very few concerns were expressed about acupuncture with only three male participants expressing concerns. Participants generally expressed the view that because acupuncture had been around for thousands of years it was a credible intervention, there was a belief that practitioners knew what they were doing and needles were sterile. Participants who had past experience of acupuncture were generally reassured through suffering no serious past adverse effects.

The concerns which were expressed were related to the qualification and hygiene of the practitioner and that treatment may be painful, may flare up PLSd or other underlying pathology. Participants were generally not afraid of acupuncture needles. Those that did not like needles talked about being accustomed to needles through their current state of health and being prepared to tolerate needles to improve health and wellbeing. Several participants viewed acupuncture needles as different from other needles and although needles per se were generally not liked, acupuncture needles were considered acceptable. There was a perception that acupuncture needles were smaller and were not inserted as deeply as other needles. One participant, despite having a fear of needles and of medical needles aggravating PLSd was willing to try acupuncture.

> *"I am afraid of needles when it comes to injections and stuff like that. But the acupuncture needles they didn't do anything to me"(P2,M,V)*

Generally, participants did not express concerns about location of needles and were 'up for anything'. Two participants expressed concerns about auricular acupuncture and scalp acupuncture because of the perception that these areas would be painful. Needling the stump / residual limb was usually not seen as any different to needling any other part of the body. Stumps required medical treatment and management and this made local acupuncture acceptable to participants. One participant expressed concerns about acupuncture around the stump as his was still very sensitive at time of interview.

> *"because I've had all sorts of things going on down there, needles and stitches,*

staples, I'd be more than happy to have needles put in there."(P7,M,T)

"I don't see why the stump would be different from any other area of the body…. I think if you can have needles in one part of the body then why not another part of the body."(P12,M,T)

Participants expressed mixed views about electro-acupuncture. It was often considered unappealing and some participants were sceptical about its benefit. Some participants were willing to try it provided there was evidence of its benefit whereas others were not willing and felt that it was not traditional.

"if I saw someone else being electrocuted first then I might say yes but at the moment definitely no, it doesn't appeal to me at all… And the Chinese used to do this thousands of years ago, I don't think so!"(P15,M,VU)

Summary of results theme 1: Understanding and acceptability of acupuncture

- Acupuncture had previously been used by a number of participants and generally there was a basic understanding of acupuncture.
- Regardless of positive or negative previous experiences participants were generally willing to try acupuncture for PLSd and had a 'will try anything' attitude.
- Few concerns were expressed about acupuncture and acupuncture needles were viewed differently to other needles.
- Scalp and auricular acupuncture did cause some concerns (pain) but acupuncture around the stump did not. Mixed views were expressed about electro-acupuncture.
- Participants were generally willing and had time to have acupuncture treatment and expected to experience a change in symptoms within a couple of weeks.

5.6.2 Theme 2: Suffering (pre-amputation)

This theme describes the extensive number of interventions, suffering and reduced quality of life many participants underwent prior to amputation. Attitudes and reasons for undergoing amputation are described.

Subtheme: treatments and management before amputation: The majority of participants reported suffering from vascular disorders or infection post trauma prior to amputation (table 5.3). Only two suffered trauma to the limb and underwent immediate amputation.

Eleven participants reported extensive periods of treatment and self-management prior to amputation with numerous unpleasant, painful and unsuccessful interventions including debridement, skin grafts, stents, external fixators, medical treatment for infection, previous amputation and casts.

> *"And they did four or five operations to that leg…. and they didn't work and then they operated again to find out why they didn't work and they operated five times…. But five operations I had in that leg before they decided to cut it off."(P9,M,V)*

Ulcers were reported by five participants of varying age and gender and caused extensive periods of painful management and treatment, with all reporting over ten years and up to 40 years of care prior to amputation. Ulcers were gruesome and unpleasant.

> *"the ulcer pain cause that was severe even when you touched it, when you cleaned it. The district nurse, he came in twice a week to do it and he had to touch it gently as possible. I used to hate the day he was coming cause I knew exactly what was going to happen…. I didn't like the days he came. Didn't look forward to them at all."(P11,M,VU)*

Seven participants had been offered or been made aware that amputation was a possibility years before undergoing amputation, allowing for time to adjust and prepare.

Subtheme: quality of life before amputation: Quality of life was reduced in all

participants prior to amputation that had not undergone immediate traumatic amputation, due to pain, and due to reduced mobility, sleep, independence and strength.

Variable levels of pain were experienced and not all participants with a history of limb pathology experienced pain pre amputation. However, all participants who suffered from vascular disorders +/- ulcers suffered intense pain which was severe and described as 'excruciating', 'a fire ball', 'fifteen out of ten', 'terrible' and 'unbearable'. It made one participant feel like committing suicide and others cry. Pain affected both sleep and mobility.

> *"I've never cried in my life but I used to lay awake and cry with it and it was terrible you know… it was so intense that I couldn't stand it any longer"(P3,F,VU)*

All eleven participants who had undergone extensive periods of treatment prior to amputation experienced reduced mobility which affected independence. This ranged from being bedbound, housebound, mobile in a wheelchair outside the home to walking independently but with a limp. Reduced mobility impacted on quality of life in different ways; from having to change occupation, to not being able to get upstairs to sleep or go to the toilet (had to urinate in bottle) to being totally dependent on another due to being bedbound so impacting on the quality of life of both the participant and the carer.

> *"I'd have to sit down on the wall, walk, walk another bit, sit down on another wall. Going down the road outside some people's houses and when I came to the bus stop I couldn't even walk from one bus stop to the other. I used to sit down at the bus stop half way toward the next one and I used to stand up by the railings wait for another five minutes and move along again"(P9,M,V)*

Subtheme: attitudes and reasons for having an amputation: Generally participants were accepting about having an amputation, due to feeling they had time to prepare, had no alternative, were aware of the risk, were glad just to be alive and had made the right decision. The participants who did not accept having an amputation had either had an unexpected sudden amputation or felt too old to be undergoing such a major procedure and expressed concerns about coping with the loss of a limb.

> *"I think when you are diabetic you know you stand a chance of losing your leg you know it's common knowledge that people with diabetes lose legs. And err, it's just something you live with…. but like I said it's just one of those things…. So anyway I thought fair enough"(P1,M,VU)*

As well as being accepting, three participants were actively positive about undergoing amputation with one requesting an amputation. Those that were actively positive had a long history of reduced lifestyle and wellbeing. Although most participants were accepting or actively positive about undergoing amputation, two were actively negative despite having had reduced lifestyle and wellbeing prior to amputation. One participant talked about being devastated and another suicidal. Age, gender, ethnicity, work status and general health did not seem to correlate to participants' attitude to amputation.

> *"I said I want it off and he said no you've got to give it more time… And all I was saying was I want it off, I want it off. So I was glad when he said come in and have it off. It was good"(P11,M,VU)*

Anger was expressed by four participants and was related to quality of care and feelings that the amputation could have been avoided. Many participants felt their amputation had come about at least partly due to poor medical care.

> *"I still say to this day if they had looked at it and said it's too hard for us or too hard to fix, and sent me to [name of hospital] in the first place, I think I would be walking about now."(P8,M,TI)*

> *"if he had sent me to the hospital first I probably wouldn't have finished with the leg off at all. The doctor he never looked at my toe, he just gave me the tablets for gout"(P9,M,V)*

Reason for having an amputation included trusting medical opinion and viewing doctors as the expert. Alternative treatment options to amputation when offered were not acceptable as there was no guarantee that they would prevent amputation and often involved further extensive surgery. Participants often felt they had reached the end of the road and all other treatment options had been exhausted. Often the limb was considered useless prior to amputation 'lump of dead meat' and amputation was chosen

to reduce pain and improve wellbeing. Other less frequently reported reasons for amputation were to resolve infection, to improve quality of life, to prevent being a burden to others and because it was the right choice at that time. Some considered refusing having an amputation. However, there was a realisation that current health status was unacceptable and this prevented them from going against medical advice.

> *"And when they are talking about they can do x, y and z but it might not work and a year down the line you will have an amputation anyway, you think I can't be messing around doing all those things when the inevitable is that you kind of need to get rid of it and start again"(P17,M,V)*

Summary of results theme 2: Suffering (pre-amputation)

- Participants had generally suffered years of pathology and undergone extensive unpleasant treatment prior to amputation.
- Ulcers particularly were gruesome, painful and caused many years of suffering and intervention.
- Quality of life was reduced in all participants with a history of limb pathology, especially due to pain and reduced mobility.
- Participants with a history of limb pathology were generally aware of the possibility of amputation and were accepting and even positive about it.
- Participants generally chose to have an amputation due to medical advice and because all other treatment options had been exhausted.
- Several participants felt amputation could have been avoided.

5.6.3 Theme 3: Acceptance and coping with the loss of a limb

This theme describes amputees' attitudes and acceptance about their circumstances, concerns around being an amputee and associated coping mechanisms.

Subtheme: attitudes and acceptance towards being an amputee: Post amputation some participants were accepting and others not accepting of their circumstances. Attitudes expressed included; feeling positive, grief, depression, regret, shock, a feeling that

amputation was not a cure to the underlying pathology, feeling of unjustness about the situation and feelings of self-worth.

> *"It's like a dead body really. It's gone and I can't retrieve it that's it."(P2,M,V)*

> *"am I less of a man, can I still pick her up and carry her to bed you know what I mean…. you feel like you've been emasculated in a way."(P12,M,T)*

The four participants who had no or little time to prepare for amputation generally expressed difficulties in accepting their situation. One described how the circumstances surrounding his amputation made it harder to accept (hit and run accident). The exception to this was a participant who was accepting of circumstances and positive in his attitude as he viewed the amputation as not his most major health problem.

> *"I think I will be able to cope very well without it…. I think my addiction is more of a major problem than my leg amputation."(P7,M,T)*

Participants who had time to prepare and had a long history of unsuccessful treatment and reduced quality of life were generally accepting and positive in their attitude even if they had not been prior to amputation. There was a feeling of being able to progress and move forward with improved quality of life and several participants wished they had undergone amputation earlier. These positive attitudes correlated with participants having better mobility and less pain compared to pre amputation.

> *"I must admit when I had the operation there was this relief and this belief that I am now on the road to do something, whereas before I have just been in limbo for three years."(P8,M,TI)*

> *"I wish I had [the amputation before] because all those years of having a smelly gammy leg um would have just gone away."(P15,M,VU)*

Subtheme: concerns about being an amputee: Some participants did express concerns about being an amputee. However approximately half did not. Key areas of concern identified included; managing at home, mobility levels, employment / managing at work, being a burden to the family, ability to do hobbies, being able to physically care for children, being able to manage in public places, and being independent. Those that

did express concerns were elderly females living alone (>80yrs) or those who had physically active life styles prior to amputation (DIY, golf, gym).

> *"You then start thinking what about work, what am I going to there…… and then you think about the rent, what about the kids, what about feeding the kids, what about the car, what about the car tax, should I worry about car tax if I can't drive, should I just sell the car or buy another car, well how am I going to buy a car next time."(P12,M,T)*

> *"I'll find something [a job], something driving you know I've not lost my licence just because I've lost my leg."(P1,M,VU)*

Subtheme: doing their best: Coping strategies were employed by amputees. Ten participants discussed the importance of doing their best and compared themselves to others. Doing your best involved being determined and working through pain. Participants compared themselves to other amputees or events in the world, thinking themselves more fortunate than others. Other amputees were also used as a source of inspiration. However, one participant compared himself to other amputees negatively as he viewed himself as having worse injuries and not progressing at the same speed as others.

> *"I'm a lot younger than some of these older lads in here, so it's hard for me but it must be twice as bloody hard for them, cause they are not young men"(P1,M,V)*

> *"there was a gentleman there who had been in the Royal Marines and he had lost his limb and I watched him every day do the most remarkable things. And I thought how can you be low about things, look at this guy, it's fantastic."(P10,M,TI)*

Three participants reported trying to keep a positive mind-set, not letting themselves go into a 'black cloud' or negativity, not letting the amputation get 'on top' of them and hoping for the best. Friends and family were considered important by six participants to provide love, help with decision making such as moving home, practical aspects of life such as bringing things into hospital, visiting and providing praise and support on progress. All those who considered friends and family important were either married or

had children.

Participants also reported other methods of coping with their circumstances including relying on faith, talking things through, finding a quiet place to clear the head and trying not to think about what had happened. Some participants set themselves goals. These included getting back to work, getting to the bus stop, getting a mobility scooter, being able to help with house work, being able to get to the local shop, getting back to playing golf, and being able to walk normally without a limp.

Summary of results theme 3: Acceptance and coping with the loss of a limb

- Participants with a long history of limb pathology prior to amputation were generally more accepting and positive about their circumstances than those with a short/ no history of pathology.
- Frequently reported positive outcomes from amputation were being able to progress and move forward with improved quality of life and reduced pain.
- Participants expressed a range of concerns about being an amputee with elderly females and males who were physically active prior to amputation expressing the most concerns.
- The most frequently employed coping strategies employed were doing your best and comparing self to others.

5.6.4 Theme 4: Real and physical phantoms

This theme describes the location and experience of PLP and PLS, its onset and the physicality and the realness of the phantom.

Subtheme: describing phantom pain: Thirteen participants experienced PLP in the distal portion of their limb. Most reported suffering pain in the foot but some reported pain in the toes or ankle. Two reported the phantom pain spread proximally and two felt pain throughout the whole limb despite one experiencing localised pain in the foot only pre amputation. Location of pain was described very precisely. Telescoping was reported by one participant.

> *"Well you know when you get a pain on your foot and you know exactly the part of the foot it is. You know, whether it's your toes or whether it's where your ankle is, under the side of your foot, um you know exactly what part the pain is…... I know exactly where the pain is you know all the time."(P15,M,VU)*

PLP was perceived as real and physical as if it still belonged to the intact body. Numerous descriptions were used to describe the quality of the pain (table 5.4). PLP was usually described metaphorically and revealed suffering. The most commonly described quality was the feeling of the phantom being tightly bound / in a vice and squeezed. Several participants also described feelings of standing on a nail or being stabbed by needles in the missing limb. Most participants tended to describe a whole variety of qualities of pain rather than just one.

> *"[the phantom] is in a vice and somebody's turning the handle round and gradually it gets more compressed and more compressed um and the pain gets stronger and stronger and as I said you can't do anything about it"(P10,M,TI)*

> *"I feel as though, at the moment the sensation I get is I feel as though my foot is tightly bandaged and I can't do much about it…. it's odd it's as though I want to undo the bandages and make the feeling go away"(P16,F,TI)*

The majority of participants felt the PLP was nothing like pain they had experienced in the past (pre-amputation) either in quality or location and only three participants thought it was similar. Alongside pain participants also talked about experiencing non-painful sensations such as pins and needles, itchiness, fuzziness and tingling in the missing limb.

Table 5.4 Qualities of phantom limb syndrome

Qualities / Descriptions of phantom limb syndrome	
In something too tight (too small shoe, in a vice, tight bandages, rope, elastic, cement and cast)	N=7
Needles / nail (standing on a nail or being stabbed by needles)	N=3
Pins and needles	
Debris in foot / shards of glass / shrapnel pebbles	N=2
Shooting	
Cramp	
Toothache	N=1
Electric impulses	
Ordinary achy pain	
Cold / freezing	
Burning	
Throbbing	
Biting (been bitten by someone)	
Gout	
Distorted toes (twisted and bent backwards)	
Sharp	
Like been hit by a brick	
Tissue been severed	
Scratching / itching	
Tingling	
Numb	

Subtheme: severity of phantom pain: Participants generally reported that phantom pain started immediately or within a couple of days and all reported that the pain started within one and a half weeks of the amputation. PLP was described as constant by nine

participants. Eight experienced sudden jolts of pain which were often outwardly visible, making participants grimace or catch their breath. One participant experienced pain gradually building and subsiding in peaks and troughs.

> *"I just kind of jolt a little bit….. And they can be quite, it's like having hiccups. You have one then another one, then another one"(P7,M,T)*

> *"all of a sudden it was really sharp jolt of excruciating pain but it would only last a few seconds. Then it would happen over and over again, probably ten times an hour. It was awful."(P15, M, VU)*

Participants described varying intensities of PLP ranging from very mild / a discomfort to off the scale, excruciating pain. Intensity of pain experienced was not dependent on intensity of pain experienced pre-amputation, underlying pathology or demographics such as gender, ethnicity, age or general health:

> *"it's a discomfort. You know, it's something you could live with."(P6,M,V)*

> *"I did say once if I had a, I know its stupid thing to say, but if I had an axe I would chop the foot off. That's how bad it is. But of course I haven't got a foot to chop off!"(P13,F,TI)*

Many participants felt the phantom pain had improved since onset but was not necessarily still improving. Six participants reported changes in quality and location of pain, feeling an increased variety of sensations, the pain moving more distally or proximally and covering a larger area of the missing limb.

Subtheme: stump sensations: The majority of participants reported having no or minimal stump pain. Only one participant felt that stump pain and PLP were related but another reported that PLP only started after the stump pain had resolved.

Subtheme: realness of the phantom: Participants generally had a very real perception of the missing limb. All except one described some feeling of the limb still being present. Participants talked about forgetting their limb had been amputated and trying to move the phantom limb out of the way, trying to physically touch the phantom and trying to use the phantom. Five talked about forgetting the limb had been amputated when

mobilising and one participant had fallen because of this. Seven talked about trying to use their limb, including trying to itch / scratch the residual limb, get something off the floor and take a shoe off the residual limb. However, one participant reported being always conscious that his limb was not there.

> *"I will be taking off this shoe and I will be trying to, be putting this foot you know, like how you put the foot to take it off, I do that a lot of the time"(P14,M,TI)*

> *"first of all I think to myself it's not giving me any satisfaction at all this scratching what's going on you know. And I lift up the sheets and of course there's nothing to look at."(P10,M,TI)*

Five participants were able to feel their phantom in minute detail and two reported feeling sensations such as pressure through their phantom.

> *"I've got toe nails as well, you know, on this one….I feel as if I've got a shin there, and toenails and an ankle"(P3,F,VU)*

> *"And I like to push it [the phantom], I can feel it pushing into the board thing at the end of the bed."(P13,F,TI)*

Subtheme: ability to move phantom: Participants could move their phantom to varying degrees from being able to move it freely to being unable to move it. Those who were unable to move their phantom had a long history of limb problems and immobility prior to amputation (one spending extensive time in an external fixator). Those who reported restricted mobility in their phantom had not necessarily had reduced mobility prior to amputation in that part of the limb. One participant felt increased effort was needed to move the phantom and another could only move certain parts of the phantom, being able to move the ankle but not the toes. Four participants were able to move their phantom freely despite not necessarily being able to move their limb freely prior to amputation.

> *"I did actually try with my eyes shut, thinking I'm going to move that leg and it was awful because I couldn't….. I can't stretch my leg out. You know, I can't do anything with it. It's just like its set in concrete"(P8,M,TI)*

I feel like I can open the toes and spread the toes….. I can sit there and move the toes up and down and left and you know, I'm doing it now! (P12,M,T)

Six participants experienced a change in perception of where the phantom limb was in space and distortion of the phantom. Others reported sensations that the phantom moved slower than expected in space.

"my foot would be turned round and gradually my toes would crunch in on themselves until they couldn't crunch anymore…. and of course your toes couldn't possibly do that, they would break if they tried to go backwards, so it would never happen as a reality type of thing but that's what it felt like."(P10,M,TI)

Subtheme: effect of prosthesis on the phantom: Four participants all of whom had been active and able to walk pre amputation, found their phantom felt more real when wearing a prosthetic. Participants reported feeling sensations such as the foot being inside the prosthetic shoe and of having a limb. Participants often liked these feelings.

"I said I think that's my foot that I had back there."(P14,M,TI)

"It's kind of almost like a nice sensation because it makes you feel like that is your foot more you know"(P17,M,VU)

Summary of results theme 4: Real and physical phantoms

- PLP was usually experienced in the distal limb and described as feeling the limb was tightly bound, in vice or being tightly squeezed.
- PLS was usually described as pins and needles, itchiness or fuzziness.
- PLP caused bursts or jolts of pain which were severe and observable.
- Phantoms felt real; limb felt present, forgot limb had been amputated, feeling the phantom in minute detail, feeling sensations through phantom.
- Phantoms had varying degree of mobility and could also feel distorted.

5.6.5 Theme 5: Living with a phantom

This theme describes attitudes towards PLSd, effects of PLSd on quality of life and management of PLSd. These were grouped under one theme because they all described how PLSd affected amputees on a daily basis.

Subtheme: attitudes towards the phantom: Participants who suffered severe PLSd generally felt negatively towards it and PLSd was often considered annoying / frustrating as pain was in a limb which was no longer there acting as a constant reminder of circumstances.

> *"I pity anybody that has this because it's no fun honestly. You know you've been through hell and back to get here and then it leaves you with this phantom pain as well you know."(P8,M,TI)*

> *"but it was so annoying. I mean how could I have a pain down there. It was so annoying!"(P9,M,V)*

PLSd was also considered bizarre, weird, fascinating, strange, marvellous, cool and amusing and four participants were actively positive about experiencing PLSd. These participants generally had intermittent pain which was improving over time, and had suffered severe pain due to vascular problems / ulcers pre-amputation. Participants felt positively because the pain was not seen as a problem, was seen as good pain or participants just felt glad to be alive and able to feel something.

> *"I don't want it to go away completely because it makes it [the prosthesis] feel more real."(P17,M,VU)*

> *"it's just there, it's trying to tell me where my foot is, which is good. So, it's good pain if that makes sense."(P15,M,VU)*

Subtheme: aggravating and easing factors: Participants reported a wide variety of factors which aggravated and eased PLSd (table 5.5). Exercise and lack of occupation were the most commonly considered aggravating factors. Exercise could both aggravate and ease symptoms with seven participants reporting exercise / using a prosthesis helped. Nine participants found distraction was an effective method of decreasing

symptoms and a variety of techniques were employed (table 5.5). However, despite participants recognising that distraction helped, participants were not always able to distract themselves.

> *"I was told by a couple of doctors that you should try and think about something else because it's all happening up here in the brain and I've tried to get my mind on other things like reading the paper or looking at TV or whatever but I can't concentrate on it because this pain just kills it."(P10,M,TI)*

Twelve of the participants passively put up with and accepted PLSd. This was generally due to the feeling that because the pain was in a phantom limb there was nothing that could be done. Others tried not to worry about the pain, worked through the pain and compared their pain to others.

> *"Because there's nothing there, there's not much I can do….. I just accept it."(P6,M,V)*

Table 5.5 Phantom limb syndrome aggravating and easing factors

Aggravating factors		Easing factors
	N=9	Distraction (walking, exercise, rehabilitation, watching TV, being occupied, working, talking to people, eating)
	N=7	Exercise and using prosthesis
	N=6	Stump techniques (shaking, rubbing / massaging, hitting the stump)
Exercise / lack of exercise Lack of occupuation	N=3	
Thinking about PLP / talking to others about PLP Being in a hospital environment (seeing needles and blood) Tiredness	N=2	
Sitting in a wheelchair Pain in the contralateral limb State of mind / mood Going to the toilet Cold Knitting Hunger Anticipation of someone knocking the stump Walking on uneven surfaces Unknown	N=1	Rest Medication Moving the phantom e.g. move phantom ankle up and down Moving residual limb (bending and straightening the knee)

Generally participants reported symptoms were worse in the evening / night time or that there was no pattern. Approximately half of the participants reported their PLSd was improving or resolved. However, the other half reported their PLSd was staying the same even if it had improved initially or was getting worse. Participants who reported that PLSd had improved were not always sure why (medication, time or just getting used to it). Those who reported PLSd was not improving had long histories of pathology though not necessarily pain pre amputation, reported pain which was >4/10 intensity, suffered episodes of intense pain and were of mixed gender and age.

Subtheme: medication and non-pharmacological interventions: All participants who knew what medication they were on reported taking gabapentin. Additional medications taken included oramorph, tramadol, oxycontin, paracetamol, fentanyl patches, morphine sulphate and amitriptyline.

Although some reported medication helped with pain, equal numbers reported that it did not and a couple were unsure whether it was helping or not. Those that reported medication helped found it beneficial to different degrees. Six participants reported medication only helped for a couple of hours (between ½ hour to 6 hours). Generally participants who found medication helpful were younger males, but this was not always the case.

> *"they've said you are on as much medication as you can be on really and it's all the sort of stuff that helps hopefully treat phantom pain. It's not touching it yet."(P13,F,TI)*

Four participants reported side effects of medication including drowsiness / falling asleep and having a dry mouth. Additionally four participants of varying demographics did not like taking medication. Non-pharmacological treatments were not commonly utilised. Two participants had tried the component of GMI, left right discrimination, but were not sure of its benefit and had only done minimal amounts. One participant had prism glasses but found them ineffective.

Subtheme: effects of phantom pain on life: Approximately half of participants interviewed had problems with sleep due to PLSd and all those that had problems with

sleep had intensity of pain which could go up to ≥7/10 intensity. Those who reported good sleep tended to have lower intensities of pain unless taking medication to help sleep, but this was not always the case. Older participants seemed to report better sleep than the younger participants. Participants reported poor sleep impacting on their daily lives in a variety of ways including; not doing well in physiotherapy, low mood, being tired and poor decision making.

> *"Makes me feel I'm not doing as well in the physio. It lowers my general mood not sleeping. For me lack of sleep brings on real negativity. So it brings on a lot of negative thoughts."(P7,M,T)*

Although the majority of participants found PLSd did not affect rehabilitation four participants of varied demographics found it did.

> *"I don't want to carry on [with physiotherapy] because it's hurting me. I want to sit down, I want to finish the session early. I know this is my only session for the day, I know when I finish today I won't have another session till tomorrow but it hurts so much that I can't do it."(P12,M,T)*

Four participants of varying age, gender and intensity of PLSd did not find PLSd affected wellbeing or mood but all the others did. All those who reported PLSd did not affect mood or wellbeing reported good sleep or just waking to turn over in bed and pain that did not affect rehabilitation, and all those who reported PLSd affected mood or wellbeing, reported PLSd that affected either sleep or rehabilitation or both. PLSd caused worrying, dark thoughts, depression, feeling 'miserable and down' and made participants act illogically and be withdrawn. Feelings could be mild 'sod this it's doing my head in' to severe.

> *"when it gets really bad I don't want to do anything. I don't want to eat, I don't want to do anything at all. I just want to be free of the pain. Um and if I was on the second floor of a building I'd probably want to jump out of the window because the pain just gets so much you can't cope with it."(P10,M,TI)*

PLSd affected activities of daily living, state of mind and concentration and was considered tiring and wearing. Additionally, three participants reported PLSd (two of

whom were married) affected their relationships with others through being in no mood to talk to anyone, being snappy, irrational and less patient with others.

> *"Cos you are in pain … you become irrational, you become snappy, you become less patient with people even though you may not have a reason for it."(P12,M,T)*

Summary of results theme 5: Living with a phantom

- Participants had both positive and negative attitudes towards PLSd.
- Amputees usually accepted PLSd due to a feeling that nothing could be done.
- Lack of occupation / thinking about PLSd was a commonly reported aggravating factor and distraction an easing factor.
- Medication usually gave some but not total relief of symptoms.
- PLSd often affected sleep, mood and wellbeing.
- Physiotherapy / rehabilitation usually helped decrease or relieve PLSd.

5.6.6 Theme 6: Being informed

This theme describes participants understanding of PLSd, expectation and access to information.

Subtheme: understanding of PLSd: Participants generally expressed understanding that peripheral nerve damage due to amputation would result in pain and cortical influences were always included. However, understanding was not always scientifically grounded, suggesting information provided on PLSd was inadequate or not clearly understood.

> *"You know if you cut through all of those nerves and those nerves still think there are feet and toes and there's legs there it's quite confusing for the nerves, very confusing for the brain. So it all makes sense why the pain is there."(P7,M,T)*

Three participants all of whom were British, white males of varying educational background expressed views that mental state was a contributing factor or cause. Four participants referred to PLSd as imaginary. One participant associated PLSd with their body / brain trying to connect with the missing limb.

"I thought I won't get that. Idiots get that. I just thought its only mental people who get that….I just took it as a mental thing"(P8,M,TI)

"I think it wants some kind of connection with the lower leg….. it throws itself downwards as though the other leg was there because then, then you feel that it's making some kind of connection with the other leg."(P2,M,V)

Participants who experienced the same location and quality of pain post amputation as they did pre-amputation were able to relate to their symptoms better than those who did not.

Subtheme: expectations: Generally participants either expected or were not surprised to have PLSd. Of those who did not expect to suffer PLSd were participants who initially thought it was a 'mental thing'. Generally participants thought PLSd would resolve but appreciated it would take time (years). These expectations often arose from speaking to other amputees. Three expressed no expectations / didn't know what to expect and this made coping with symptoms harder.

"for 26 years there's been the other part of my leg and my ankle and my foot and so I can understand why there is this period where it's taking a long time to get used to the sudden change."(P7,M,T)

"So when I spoke with the guy with four years amputation, four years, he still feels it. So I told myself I say you will experience it after four years."(P14,M,TI)

Subtheme: communication: Participants felt there was a lack of access to information, eavesdropped on doctors' conversations and had difficulty accessing doctors. Information which was provided was inadequate and often did not come from the medical team. Participants and their families had to seek out information and information was shared.

"The only people who have explained it to me is other patients. But no doctors or nothing mentioned anything to me about the pain."(P9,M,V)

"One of the registrars did come and see me and said that some patients feel something called phantom pain, here's a leaflet have a nice day….. [but] you want

to actually talk to a person. Um but yes I got a little fold out leaflet about phantom pain."(P12,M,T)

A number of resources were used to obtain information on PLSd including; the internet, especially U-tube by younger amputees, war films and books. Families were needed to access information when the individual could not access it directly. Participants often talked to other amputees about PLSd and this contributed to participants' expectations of PLSd (see above). Those who did talk to others usually found it helpful and several talked about sharing advice with others. However, some did not find talking to others helpful, with one participant reporting feeling like the expert and another reporting not getting any definitive answers.

Summary of results theme 6: Being informed

- Participants had a varied understanding of PLSd. Some despite having some understanding of peripheral nerve damage and cortical influences felt it was 'imaginary' pain or due to mental state.
- Participants generally expected to have PLSd and expected it to last for years.
- Participants generally felt that not enough information was provided on PLSd and actively sought out information.

5.6.7 Theme 7: Outcome measure preferences

All participants preferred the Short Form McGill Pain Questionnaire 2 (SF-MPQ-2) to either the Neuropathic pain scale (NPS) or the Neuropathic pain symptom inventory (NPSI). Feedback on the SF-MPQ-2 is shown in table 5.6. Generally participants found the SF-MPQ-2 relevant, easy to understand and complete and some participants liked the fact that the questionnaire was only on one sheet of paper. However, although some participants found the questionnaire appropriate, others found there were too many descriptive qualities and one participant struggled to understand the difference between the different pain qualities described.

"this is really interesting because you've put 22 things here and I can relate to most of them. So I think this one would be really useful…. I think there is only a couple which I'd put one or zero for and I think nearly 20 out of 22 I would be able to rate four or over."(P7,M,T)

"I would say of it…. for me, there's too many feelings, different feelings and that."(P13,F,TI)

The majority of participants preferred the EuroQol-5 Dimensions (EQ-5D-5L) to the brief pain inventory because it was considered the simpler of the two. However, two participants did find the final question 'we would like to know how good or bad your health is TODAY' difficult to answer. This is because participants felt that they would answer differently depending on whether they focused on general health or PLSd in their feeling of health.

"I think I probably answered it wrong because I was thinking of when it says health I was thinking of pain more. And obviously this is whether you are healthy or not in which case the score should be higher"(P10,M,TI)

Participants generally managed to complete the outcome measures without prompting or help within 20 minutes.

Summary of results theme 7: Outcome measure preferences

- The numerical rating scale (NRS), short form McGill Pain Questionnaire 2 (SF-MPQ-2), insomnia severity index (ISI), hospital anxiety and depression scale (HADS), perceived stress scale ten item (PSS-10), patient global impression of change (PGIC) and EuroQol-5 Dimensions (EQ-5D-5L) were identified as appropriate outcome measures for use in the planned feasibility study, described in the next chapter.

Table 5.6 Feedback on outcome measures considered for the feasibility study

Outcome measure*	Participant comments (positive)	Participant comments (negative)
Numerical Rating Scale (NRS)	Appropriate and relevant (P1-17)	Need to make it clear that the scale is measuring PLP / not other body pains P1
Short-Form McGill Pain Questionnaire – 2 (SF-MPQ-2)	Easy to understand and complete P1,2,6,8 The whole questionnaire is on one sheet of paper P1,8 Using a 1-10 scale follows on well from the numerical pain rating scale P1 It has plenty of options P2 Able to relate to most of the options P7 Relevant P7	Unable to fill in – did not understand P12 Too many descriptions P13,15 Repetitive P14
EQ-5D-5L	Gives a full range of options (for example from not being able to walk to being able to walk with no problems) P6 Easy to complete P7	Hard to give score for 'health today' as generally feels well apart from amputation / PLP P8,10 Difficult to answer mobility question as able to walk with a prosthesis in physiotherapy but not otherwise. P10
Insomnia Severity Index (ISI)	Easy to complete P7 Appropriate and relevant P13,15 (Hospital environment and medication may affect sleep) P8,10,17	May not get a meaningful result as factors other than PLP may be affecting sleep P1,2 Did not answer question on how noticeable to others do you think your sleep problem is as felt unable to answer this P12
Hospital Anxiety and Depression Scale (HADS)	Relevant P7,12,15	Found a few questions hard to understand P13 Refused to fill in the questionnaire as felt it was inappropriate P14
Perceived Stress Scale ten item (PSS-10)	Relevant P7,12,15	Refused to fill in the questionnaire as felt it was inappropriate P14

Note: *Further details of the outcome measures are provided in section 6.5.4.

5.7 Discussion

5.7.1 Theme 1: Understanding and acceptability of acupuncture

Most participants had a basic understanding of acupuncture. This was unsurprising as acupuncture is now widely utilised and routinely prescribed in healthcare, including within the NHS, and has been recommended in NICE guidelines (NICE, 2014). However, prior to this study very little was known about the acceptability of acupuncture for the treatment of PLSd. Acceptability is important as it impacts on the take-up, compliance and willingness to see the treatment through (Hopton *et al.*, 2013). The results of this study suggested acupuncture would be an acceptable and feasible intervention for PLSd in an inpatient rehabilitation setting.

Participants were generally willing to try acupuncture, or any intervention which may help resolve PLSd and were also willing to be involved in a trial. Acupuncture was considered as acceptable as other interventions. Although all participants in this study were receiving pharmacological intervention, few reported receiving non-pharmacological interventions for pain relief (physiotherapy focused on rehabilitation), and this may be partly why acupuncture was considered so acceptable. Additionally, as pharmacological treatments are not necessarily effective (section 2.6.2.3), this may possibly make alternative non-pharmacological treatments more appealing.

Other studies exploring the decision making process around acupuncture discuss why people decide to try acupuncture and issues surrounding finding an acupuncturist (Bishop and Lewith, 2013). As acupuncture would be offered to participants involved in the feasibility study, these barriers would be removed. Additionally participants in the feasibility study would not have the burden of either funding their treatment or having to travel for treatment, which probably would also make it more acceptable.

Participants in this study ranged from 26 to 84 years. Age did not seem to be a factor which influenced acceptability of acupuncture. Other studies have found acupuncture to be acceptable in elderly people suffering from chronic pain (Couilliot *et al.*, 2013) suggesting acupuncture may be tolerable across different age groups. Hanley *et al.* (2006) reported that some amputees with PLSd may believe their symptoms to not be

severe enough to warrant treatment, with those experiencing less pain and disability feeling less in need of treatment, and this was also found to be the case in this study.

Previous studies have reported needle related discomfort, temporary worsening of symptoms, tiredness and financial costs as barriers to treatment (Hopton *et al.*, 2013). This study identified barriers to treatment, including concerns about treatment being painful and flaring up PLSd or other underlying pathology. Despite these concerns, participants were still willing to try acupuncture, possibly due to lack of alternative treatment options.

Participants did not express concerns about receiving acupuncture around the stump. Studies have reported that stump pain is common post amputation, it can persist beyond the stage of healing (Nikolajsen, 2012) and amputees can feel mutilated post amputation (Murray and Forshaw, 2013). However, in this study this was not the case and participants were generally unconcerned about receiving acupuncture around the stump. This finding supports including the option of local needling around the stump in a feasibility study as recommended in the Delphi study protocol (figure 4.7).

Participants expressed mixed views about electro-acupuncture. Despite electro-acupuncture being beneficial for the treatment of persistent neuropathic pain (Zhang *et al.*, 2014) it was viewed as unappealing and unauthentic. The option for using electro-acupuncture in the feasibility study (Chapter 6) was retained as participants' attitudes towards electro-acupuncture may change post commencement of acupuncture intervention. However, practitioners were advised not to use it initially because of participants' perceived lack of willingness towards this type of acupuncture intervention.

Participants generally felt it would be feasible to receive acupuncture a couple of times a week. The protocol developed from the Delphi study (figure 4.7) suggested treating weekly or twice weekly and reducing frequency of treatments as symptoms abate. Therefore, in the feasibility study (Chapter 6) frequency of treatment was set at twice weekly. A flexible approach was taken to treatment in the feasibility study to avoid acupuncture clashing with other hospital appointments.

Participants generally expected to see a reduction in symptoms over the course of a couple of weeks, suggesting that participants would be willing to have several treatments and not drop out if improvement was not noticed immediately.

5.7.2 Theme 2: Suffering (pre-amputation)

The majority of participants underwent dysvascular amputation. This is a chronic condition causing pain, requiring extensive management and impacting on daily lives (Gibson and Kenrick, 1998). These experiences were captured in this study.

For many individuals adjusting to amputation occurs long before the actual surgical procedure (Hamill *et al.*, 2010) and this was found to be the case in this study with many participants coming to terms with and accepting amputation prior to the actual event. This was probably due to the majority of participants having a long history of pathology and awareness of possible amputation and therefore time to prepare and adjust. Studies report amputation can be viewed as bad or difficult (Chini and Boemer, 2007) evoking feelings of sadness, shock, surprise, unacceptance, anger and suicidal thoughts (Senra *et al.*, 2012, Livingstone *et al.*, 2011). Although some participants in this study expressed these emotions, most were generally accepting and even positive about undergoing amputation. This was probably due to their long history of pathology and suffering pre-amputation. The positive attitude towards amputation found in this study is not unique and has been reported in other studies. Couture *et al.* (2011) reported acceptance and happiness about undergoing amputation due to the expectation of it resolving pain and Chini and Boemer (2007) found amputation was viewed positively due to the expectation of it resolving pain, stopping disease and avoiding death.

A subtheme which emerged during the interviews (section 5.6.2) was the lack of satisfaction with medical care and a feeling that amputation could have been avoided. Livingstone *et al.* (2011) also found participants reported poor consultation, incorrect care and lack of expertise of some health care professionals and Gibson and Kenrick (1998) suggested the goals of acute care fail to address the needs of patients with chronic conditions. Participants in this study who were dissatisfied with care did not necessarily have chronic conditions at the time of feeling dissatisfaction. Dissatisfaction with care often evolved from the participant's lack of satisfaction with the perceived

expertise of some health professionals.

5.7.3 Theme 3: Acceptance and coping with the loss of a limb

A theme which emerged during the study was acceptance about losing a limb. Losing a limb is not always acceptable and amputation has been reported to cause feelings of emptiness (Sjodahl *et al.*, 2004) anxiety, depression, social discomfort and body-image anxiety (Senra *et al.*, 2012). In this study, difficulty in accepting the loss of a limb was unsurprisingly associated with participants who had no or little time to prepare for amputation. However, participants who had time to prepare for amputation were generally accepting and positive about having an amputation. This was probably due to these participants having improved or no worse quality of life post amputation. Other studies have also found that amputation can be a positive experience, allowing the person to return to life and living (Chini and Boemer, 2007). A study of dysvascular amputees found 69% appraised their amputation as a positive experience, with below knee amputees more likely to appraise their amputation positively than above knee amputees (Couture *et al.*, 2011).

In this study, amputation level did not seem to affect attitude to amputation, possibly as level of amputation did not necessarily correlate with level of mobility, but functional independence / improved mobility and reduced pain did. Social discomfort was not identified in this study possibly due to all participants being inpatients at time of interview, meaning they had not been exposed to experiences outside a hospital setting. Sjodahl *et al.* (2004) reported amputees may suffer feelings of mutilation but this was also not identified possibly due to the study environment normalising stumps and disfigurement.

Similar to other studies, some participants did express concerns about coping with the loss of a limb (Livingstone *et al.*, 2011) and these concerns were expressed by both older and younger amputees. Although concerns were not age specific, different age and gender groups expressed different concerns. Approximately half of participants did not express concerns. This may be due to many participants having lived with a non-functional limb prior to amputation and having improved mobility and independence post amputation.

Coping refers to the behavioural, cognitive and emotional effort to maintain balance between a person and the environment and is used to regulate distress and improve the situation (Sjodahl *et al.*, 2004). The most frequently employed coping strategies identified in this study were doing your best and comparing self to others. Post amputation, deciding to stay positive has also been identified by Livingstone *et al.* (2011) and Murray and Forshaw (2013). Comparing self to others has also been identified in other studies but labelled as 'downward comparison coping' which compares oneself with those less fortunate (Sjodahl *et al.*, 2004, Hamill *et al.*, 2010). In this study participants also identified personal goals. Goal setting has been found to be a strategy often adopted by amputees in attempts to reassert independence (Hamill *et al.*, 2010).

5.7.4 Theme 4: Real and physical phantoms

Participants generally experienced pain in the distal portion of their limb. This is in keeping with other literature (Nikolajsen, 2012) and is due to PLSd being experienced in places with the most extensive innervation density and cortical representation in the somatosensory cortex (Hill, 1999). Participants reported pain which was 'real' and 'physical' and could be described very precisely in terms of location. The precision of the location of pain is not captured in quantitative studies and past qualitative studies have been of poor methodological quality, reducing the trustworthiness of findings.

Numerous descriptions were used to describe the quality of PLP which were often similar to those described in other studies (sharp, tingling, shooting, stabbing, throbbing, burning (Ehde *et al.*, 2000, Katz, 1992)). However, in this study most participants also described their experience of PLP metaphorically giving a vivid picture of suffering endured, and emphasising the reality of the experience. The most commonly described quality of PLP was spontaneously described as the phantom limb being squashed, tightly bound or squeezed. This quality is not commonly reported and may not have been captured in other studies as it involved a detailed description rather than just a word or phrase to describe the quality of the pain.

Participants generally reported PLSd which started within a couple of days of amputation and was constant but of varying intensity. This was unsurprising as similar findings have been reported in multiple studies (Nikolajsen, 2012). However, it also

emerged that PLSd can come in sudden severe jolts which can be outwardly visible. This is not reported in PLSd literature.

Stump pain was not commonly reported. This was not expected as stump pain and PLSd are recognised as an inter-related phenomenon (Ketz, 2008, Richardson *et al.*, 2006). However, all participants in this study regularly self-massaged / desensitised the stump and this may explain the low occurrence of stump pain.

Kinaesthetic perceptions were reported by some participants and one participant experienced telescoping and two altered sensation of where the limb was in space. With telescoping, the shape and position of phantom usually changes over a timeframe of many months, with the distal limb telescoping inward towards the stump (Devor, 1997). Telescoping may be due to changes in receptive fields. The extent to which cutaneous input from the stump and surrounding tissue occupies the somatosensory cortex previously utilised by the amputated limb may affect telescoping and telescoping may act as a perceptual marker of cortical changes (Katz, 1992). Telescoping was probably not experienced by more participants in this study due to the short time frame between amputation and interview.

A recurrent theme which emerged during the interviews was the 'realness' of the phantom. Participants generally experienced that the missing limb still felt real and present. This has been described only briefly in other qualitative studies (section 2.5.3.2) so these findings extend the understanding of this phenomenon. These experiences may partly be due to changes in cortical representation in the somatosensory cortex and partly due to motor commands and the parietal lobe containing one's body image (Ramachandran, 2005). Body image is the internally constructed ensemble of experiences and internal image and memory of one's body in space and time. The neural circuitry for body image is laid down partly by genes and can survive indefinitely even when one receives contradictory information from the senses (Ramachandran, 2005).

As well as experiencing exteroceptive and kinaesthetic perceptions, participants also reported kinetic perceptions. This phenomenon has been reported in other studies (Mortimer *et al.*, 1998). However, in this study although some could move their

phantom freely, others could not and those with a history of restricted mobility pre-amputation could not always move their phantom post amputation. As with kinaesthetic perceptions, kinetic perceptions may be explained by the convergence of information from body image, the motor cortex and the somatosensory cortex (Ramachandran, 2005). Paralysis of phantoms may be due to a memory of the paralysis being carried over to the phantom limb (Ramachandran, 2005).

Several participants reported wearing a prosthesis made the phantom more real. Murray (2004) also found that the phantom and prosthetic could interlace into a phenomenal corporeal structure and that the phantom could aid the use of a prosthetic.

5.7.5 Theme 5: Living with a phantom

PLSd was sometimes viewed as a positive experience. Pain is usually perceived as an unwanted experience and it was not anticipated that some amputees would not want it to resolve. As stated above a phantom can aid prosthesis use, and awareness of the fact that PLSd may be viewed positively should be taken into account before trying to treat / resolve it. However, this study only captured amputees' early experience of PLSd. Later experiences of PLSd may be different.

Aggravating factors frequently included lack of occupation, thinking about PLSd and exercise. Lack of occupation and thinking about PLSd may cause emotionally triggered pain where exposure to isolated aspects of memories related to amputation revoke or worsen associated PLSd (Giummarra *et al.*, 2011). Pain may also have been triggered by observing or thinking about another's pain due to disinhibition of pain mirror systems meaning neural systems which are active when processing one's own pain are active when processing others' pain (Giummarra *et al.*, 2011). Other factors may have aggravated PLSd because of increased efficiency or amplification of neurological response in various nerve structures (Melzack, 1992), and because of somatosensory maps and cortical reorganisation. For example one participant found going to the toilet aggravated PLSd. This may be due to the genitals being next to the foot in Penfield's homunculus (Ramachandran, 2005).

Distraction was reported to ease PLSd and both distraction / exercise and stump

techniques were self-management methods frequently employed. Distraction may help reduce emotionally triggered pain due to the mechanisms described above. Stump techniques may be effective through reducing muscle tension in the residual limb (Giummarra *et al.*, 2011) and through stump desensitisation; nociceptive input from the residual limb and ectopic discharge from stump neuroma have been postulated as peripheral mechanisms contributing to PLSd (Flor, 2002) (section 2.4.1).

Mindfulness is the practice of cultivating a state of metacognitive awareness of the present moment including one's thoughts, emotions, sensations and perceptions (Garland, 2014). Through intentionally focusing on pleasant events, psychological resilience may be promoted (Garland, 2014) and mindfulness has been shown to be beneficial in reducing pain intensity and improving pain coping in chronic pain management (Day *et al.*, 2014). This may be a technique which could be taught to amputees for self-management of PLSd especially when distraction is unsuccessful. Participants all reported taking gabapentin frequently in conjunction with other medication but reported mixed results. As reported in section 2.6.2.3**,** the efficacy of gabapentin from placebo-controlled trials is not robust with inconsistent results reported in RCTs (Fang *et al.*, 2013). These findings suggest the need for alternative treatment approaches to manage PLSd. Non-pharmacological treatments were not commonly accessible or utilised by participants. Although research on mirror therapy and graded motor imagery for the treatment of PLSd is insufficient (section 2.6.2.5) these techniques may be effective in reducing PLSd (Foell *et al.*, 2014, Bowering *et al.*, 2013) and amputees may benefit from having improved access to these interventions.

Sleep was commonly reported to be disrupted by PLSd. Poor sleep can affect performance and productivity due to fatigue, irritability, concentration difficulties and decreased alertness. Also, a strong link exists between sleep and stress (Wells and Vaughn, 2012). Insufficient sleep is associated with the development of chronic disease such as depression, diabetes, obesity and heart disease (Balkin *et al.*, 2008). Amputation is in itself a stressful experience and amputees may already have chronic conditions such as diabetes. Poor sleep may exacerbate pathology as well as affecting performance and productivity. Poor performance in physiotherapy could affect rehabilitation and therefore discharge date from hospital, potentially resulting in increased cost to the

NHS. Although, the majority of participants did not report PLSd affected rehabilitation, some did. A non-linear association between pain intensity and function has been reported by Jensen *et al.* (2001) with higher pain intensities having a proportionally larger negative impact on function. Poor function due to pain may negatively affect wellbeing and quality of life and is associated with depressive symptoms (Bair *et al.*, 2003). PLSd affected wellbeing and mood in the majority of participants and also relationships. Pain and depressive symptoms commonly occur together (Bair *et al.*, 2003) and chronic pain (≥ 6 months) has been strongly associated with major depressive disorder (Ohayon and Schatzberg, 2003). Pain needs to be better managed in amputees to avoid the development of disrupted sleep, poor functioning, chronic pain and the associated negative effects on wellbeing and mood.

5.7.6 Theme 6: Being informed

Although participants generally did include descriptions of cortical and peripheral changes in their understanding of PLSd, there were indications that there was no thorough or 'medical' understanding highlighting the need for better education and access to information about PLSd. The passive acceptance coping strategy of PLSd also suggested a lack of thorough understanding with participants feeling nothing could be done as the pain was in a limb which was no longer there. These findings suggest there is still a lack of standardised approach to educating amputees about PLSd.

Amputees' beliefs and knowledge of PLSd have previously been evaluated. One study identified concerns about the level of information provided and that professionals did not properly prepare amputees for PLSd (Mortimer *et al.*, 1998). A subsequent study identified that information about PLSd did not always come from a professional, and that information was not always helpful (Mortimer *et al.*, 2002). No evidence supported that amputees were consistently receiving high-quality information from professionals. Mortimer *et al.* (2004) also completed focus groups and found that few professionals were fully aware of the nature or problems associated with PLSd. Findings from this study suggest that the educational needs of amputees have still not been fully addressed, with information provided being variable in quality, resulting in poor understanding of PLSd. Although participants in this study used the internet as a source of health information, awareness is needed that this could provide misinformation.

Future studies need to explore further the educational needs of amputees.

Explanation of the underlying cause of persistent pain can form the foundation of pain management. Neuroscience education describes the neurobiology and neurophysiology of pain and pain processing by the nervous system. It describes peripheral nerve sensitisation, central sensitisation, synaptic activity and brain processing as well as upregulation and downregulation modulating the pain experience (Louw *et al.*, 2011). Professionals underestimate patients' ability to understand complex issues related to pain and patients are interested in knowing more about pain (Moseley, 2003b). A systematic review indicated that neuroscience education can decrease pain ratings, increase physical performance and decrease perceived disability and catastrophising in musculoskeletal patients (Louw *et al.*, 2011). A neuroscience education approach using teaching tools such as pictures and work books could be used to educate amputees about PLSd and may potentially also help with pain management of this phenomenon.

Participants were generally unaware of possible interventions such as decreasing muscle tension in the residual limb to reduce PLSd, GMI or mirror therapy alone to reduce central sensitisation and cortical reorganisation, or stump liners to shield electromagnetic fields (weather changes may exacerbate PLSd due to individuals reacting to electromagnetic waves generated by the atmosphere which affects serotonin metabolism, which is important for descending inhibitory pain pathways (Giummarra *et al.*, 2011)). Amputees need to be informed of, understand the reasoning behind and be provided with access to the different treatment techniques available for treating PLSd to help empower them to manage their symptoms.

5.7.7 Theme 7: Outcome measure preferences

Due to feedback from participants, the following questionnaires were used in the feasibility study (Chapter 6); numerical rating scale (NRS), short form McGill Pain Questionnaire 2 (SF-MPQ-2), insomnia severity index (ISI), hospital anxiety and depression scale (HADS), perceived stress scale (PSS), patient global impression of change (PGIC) and EuroQol-5 Dimensions (EQ-5D-5L). These outcome measures are described in the following chapter (section 6.5.4). Due to feedback on the EQ-5D-5L,

participants in the feasibility study were advised that the final question was about health today, not only about PLSd. Participants were advised to complete the question on mobility with respect to how mobile they were outside of physiotherapy. It was recognised that the ISI may not capture participants' true sleep pattern in the feasibility study as sleep may be disturbed due to being in a hospital environment or altered due to changes in medication.

The one participant who refused to fill in the HADS and PSS was very distressed about his recent amputation. The researcher did not want to cause distress to participants in the feasibility study but as only one participant during the fifteen interviews refused to complete the HADS and PSS, and other participants found them relevant, it was decided to use these questionnaires in the feasibility study.

Summary of discussion

- Acupuncture was considered an acceptable intervention possibly because participants did not have some of the usual burdens affecting acceptability (cost of treatment, travel to appointment, finding a practitioner).
- Although amputees may have concerns about acupuncture, due to lack of other treatment options, acupuncture may still be considered acceptable.
- Amputation may be viewed as a positive experience in chronic conditions as it can be seen as a way to resolve pathology, reduce suffering and improve quality of life, allowing amputees to move forward in life with improved health.
- PLSd is a real and physical pain which can be described in precise detail. Participant descriptions provide insight into the experience of PLSd which quantitative studies do not capture.
- The phantom limb may feel real and present, with amputees experiencing kinetic and kinaesthetic perceptions, due to the convergence of information from body image, the motor cortex and the somatosensory cortex. Kinetic perception may be influenced by the mobility of the limb pre-amputation.
- PLSd may be aggravated by emotional triggers, increased efficiency or amplification of neurological response, disinhibition of pain mirror systems and cortical reorganisation.
- PLSd needs to be better managed (both pharmacologically and non-pharmacologically) to avoid impacting on wellbeing and causing the development of depressive disorders.
- Amputees do not have a thorough understanding of PLSd and information provided is inconsistent and often inadequate. A standardised approach to educating amputees needs to be developed. A neuroscience education approach could be considered.
- Due to feedback in this study, participants in the feasibility study were given instruction before completing the EQ-5D-5L that mobility referred to general mobility and not what could be achieved in physiotherapy and that the final question was measuring health today not just PLSd.

5.8 Reflexivity

The researcher was aware that her professional background and current position as a researcher may introduce bias. She acknowledged that she was biased towards acupuncture but strived to maintain a neutral stance through the research process. She actively chose not to disclose her professional background to participants to avoid this influencing findings. She felt that not disclosing her background, avoiding leading questions and charting data during analysis ensured she minimised this bias and portrayed participants' views as truthfully as possible.

Through completing the literature review the researcher was aware that she had preconceptions about the experience of PLSd and effectiveness of treatments for PLSd. Throughout the study she was aware of this and attempted not to ask participants leading questions. She attempted to not let this prior knowledge influence data analysis through adhering to a strict method of data analysis.

The researcher felt that although her age, gender and ethnicity did not have a large impact on the data generated during the interviews, her interview technique did. Initially the researcher did not give participants time to pause, reflect and expand on the topic being discussed. Additionally, even in later interviews, the researcher found herself sometimes running the interview at her tempo rather than at the tempo of the participant, not giving participants time to fully describe and disclose their situation / opinion. When she was aware of this she actively made herself not ask the next question until there had been a significant pause in the interview. The researcher felt the rapport during the initial interviewers may have been compromised due to her being nervous. Initial interviews were more rigid and stuck closely to the topic guide and it was only after the first few interviews that the researcher managed to develop a more conversational form of interview technique and therefore develop a better rapport with participants. On writing up memos and results, fewer quotes were included from the initial interviews than the later ones. This may be because of the poorer rapport, and therefore less meaningful data generated in the initial interviews. Although the researcher empathised with participants who were distressed about the loss of a limb, she felt she could not fully understand, having never experienced anything similar to this and felt that although most participants talked openly about their feelings, some were

withdrawn, possibly due to her not being a 'member of the group' and not willing to fully disclose their feelings. This may have affected the data generated.

A major consideration which emerged during the interview process was the direction the interviews took. Although the interviews were designed to primarily capture participants' views on the acceptability of acupuncture for treating PLSd and willingness to be involved in a RCT, in reality the researcher found participants would talk at length about their experience of amputation and PLSd, but the researcher struggled to engage participants in discussion about acupuncture and outcome measures. These areas of the interview always involved more prompting from the interviewer and generated less rich data. This may be because acupuncture had not been experienced by all participants and was not part of their current life experience. Over the course of the 15 interviews, the interviews emerged and became more about experience of amputation and PLSd and less about acceptability of acupuncture. A decision was made to include data on the experience of amputation in this study to provide a more complete picture of participants' experience and to put participants' views on perceived acceptability of acupuncture into the context of amputees' lives and living with amputation and PLSd.

5.9 Conclusion

The study provided an original and detailed account of amputees' views on the perceived acceptability of acupuncture for treating PLSd and willingness to be involved in a RCT. It identified outcome measures which could be used in a feasibility study and provided a rich account of amputees' experience of undergoing amputation and experience of PLSd.

In keeping with the sequential MMR design of this project, this qualitative study informed the feasibility study. PLSd is often burdensome and needs better management, suggesting the need for further research into effective interventions. Acupuncture was generally considered an acceptable intervention, partly due to difficulty managing PLSd pharmacologically. Participants were willing and felt they had the time to participate in a study, whilst at the ARU. Results from this study confirmed that the Delphi protocol developed in Chapter 4 should be acceptable in a feasibility study. Outcome measures were identified which could be used in a feasibility study.

The study collected rich data on the experience of amputation and PLSd. Many amputees undergo years of pathology and suffering prior to amputation and the duration and extent of suffering pre-amputation influences appraisal of amputation. Amputation can be viewed as a positive experience when it results in improved quality of life such as increased mobility, independence and decreased pain. PLSd is 'real' and descriptions provide insight into amputees' experience of this phenomenon. PLSd may be viewed positively by some amputees and can make a prosthetic limb feel more real. Kinetic, kinaesthetic and exteroceptive perceptions are experienced probably due to the convergence of information from body image, the motor cortex and the somatosensory cortex. PLSd may be aggravated by emotional triggers, increased efficiency or amplification of neurological response, disinhibition of pain mirror systems and cortical reorganisation.

This study identified possible areas for future research; explore the educational needs of amputees to ensure a better understanding of PLSd, evaluate if neuroscience education is appropriate for educating amputees about PLSd, evaluate the accessibility of non-pharmacological interventions such as GMI and mirror therapy within an NHS

setting and evaluate the effectiveness of mindfulness in the management of PLSd.

Summary of qualitative descriptive study conclusion

- Provisional data were obtained on the perceived acceptability of acupuncture and participation in a feasibility study. Findings suggest acupuncture and participation in a study would be acceptable.
- Outcome measures were identified which could be used in a feasibility study.
- Amputation was found to often be viewed positively but the complication of amputation, PLSd, was usually found to be bothersome affecting wellbeing.
- PLSd could sometimes be viewed positively and could make a prosthetic limb feel more real.
- The study identified that information provided to amputees about PLSd is inconsistent and often insufficient.

Chapter 6. Establishing the feasibility and acceptability of providing acupuncture to lower limb amputees with phantom limb syndrome

6.1 Introduction

The literature review identified that currently there is little evidence supporting the use of acupuncture to treat PLSd, highlighting the need for further research in this area. As little evidence was identified, in keeping with the theoretical framework of this project, time was spent developing an acupuncture protocol to be used in this feasibility study (Chapter 4). This acupuncture protocol, although not claiming to be 'best practice', could be considered to be 'good practice' having been developed from qualified and experienced practitioners. Also, 88.3% of participants involved in the development of this protocol agreed or strongly agreed with it (section 4.6.3), suggesting it would be accepted by acupuncture practitioners involved in a trial.

The previous study, also conducted in keeping with the MRC framework for developing complex interventions, identified that acupuncture was perceived as an acceptable intervention by lower limb amputees. The study established that lower limb amputees with PLSd in an inpatient setting would potentially consider acupuncture an acceptable intervention to treat this pathology and would consider taking part in a feasibility study. Additionally, feedback on outcome measures was obtained which helped guide the development of this study.

This study was undertaken using a MMR embedded design [QUAN(qual)]. A total of 15 participants with PLSd were randomly assigned to receive either 8 acupuncture treatments and usual care or usual care alone over four weeks. A total of 8 participants received acupuncture and usual care and 7 usual care only. Outcome measures were completed at baseline, weekly throughout the study and at one month post completion of the study. Post completion of the trial participants in the acupuncture group were interviewed about their experience. Feasibility specific data were collected and key data were integrated bringing qualitative and quantitative results together using side-by-side comparison (Creswell and Plano Clark, 2011). This chapter discusses the rationale for using an embedded MMR design, justifies conducting a feasibility study and provides an

explanation of why sham acupuncture was not included in the study design. A detailed account of the methods used, and rationale for choice of outcome measures is given. Feasibility specific outcomes are documented and findings debated. Limitations of the study are discussed. The published study protocol is included in appendix 6.1.

6.2 Objectives

This chapter addressed the project objective described in the introduction (figure 1.1):

- Evaluate the feasibility and acceptability of providing acupuncture intervention to a group of lower limb amputees in preparation for a definitive multi-centred RCT evaluating the effectiveness of acupuncture for treating PLSd.

As described in the introduction (figure 1.2) the component parts of this objective were to:

- Explore the feasibility of recruiting, randomising and retaining participants.
- Evaluate the feasibility and acceptability of having a routine care control.
- Evaluate adherence / compliance and acceptability of an acupuncture intervention.
- Explore participants' experience of completing outcome measures.
- Ascertain the appropriateness of primary and secondary outcome measures for use in future trials.
- Explore the perceived effectiveness of acupuncture for treating PLSd and other secondary symptoms.
- Generate data on sample size for use in a definitive trial.

6.3 Situating the research

The study took place at the ARU described in section 5.3 and acupuncture was provided by practitioners working within an acupuncture clinic which was co-located in the same building as the ARU. The acupuncture clinic was part of the same NHS trust as the ARU and was an established acupuncture department which had been running for over 20 years providing treatment for patients with long term conditions. It offered a course of 5-10 weekly treatments, accessed through GP referrals, for chronic pain, headaches and migraines. It also provided a self-referral system for HIV patients and drop in auricular acupuncture clinics for stress management, smoking cessation, addictions, anxiety and depression.

Staff at the clinic included 6 acupuncturists who practiced TCM style acupuncture. Included within acupuncture treatments, were the adjunctive interventions cupping, tui- na and electro-acupuncture. Pilates classes were run twice weekly and qi gong classes once weekly.

6.4 Methodological approach

Although case studies suggested acupuncture was an effective intervention for the management of PLSd (Hu *et al.*, 2014a), case studies are at the bottom of the hierarchy of evidence and are the least likely to inform practice (Daly *et al.*, 2007). Of the two controlled trials identified in the systematic review (section 2.7), both were non-randomised and were of poor methodological quality. There was therefore a need for further research to establish the effectiveness of acupuncture for the management of PLSd. Hierarchies of evidence often consider that systematic reviews and multicentre studies provide the highest level of evidence on effectiveness. In terms of research design, the validity of the results varies depending on the study design used and the RCT is considered to provide the most reliable evidence. This is because RCTs minimise confounding variables and have high internal validity (Evans, 2003). A preparatory study was therefore deemed appropriate to assess feasibility in order to inform the design of a future RCT to establish effectiveness.

6.4.1 Study design

There is no clear distinction between a pilot and a feasibility study (Arain *et al.*, 2010) and the two have been considered to be synonymous (Thabane *et al.*, 2010). However, it has been suggested that a feasibility study is research with flexible methodology which is done before the main study to estimate important parameters, and a pilot study is a miniature version of the main study with more rigid methodology, to test that components work together (Arain *et al.*, 2010). In this study, as the main objectives were to estimate important parameters, and as the outcome of interest (intensity of PLSd) was not formally evaluated the term 'feasibility study' was used.

Completing a feasibility study before a main study can increase the likelihood of the main study being successful (Thabane *et al.*, 2010) and in keeping with the MRC framework for developing and evaluating complex interventions this was considered an appropriate step in this project. Feasibility studies have different objectives to fully powered RCTs, having clearly defined objectives which estimate parameters needed to design a full trial (Arain *et al.*, 2010). These objectives include assessing the feasibility of completing the processes involved in the study, assessing resources such as time and

budget, identifying management problems such as data management and allowing for assessment of, for example, safety, response and estimation of treatment effect and its variance (Thabane *et al.*, 2010). Feasibility studies allow sample size calculation, enable procedures to be tested and allow for assessment of completion and appropriateness of outcome measures (Lancaster *et al.*, 2004). These studies are not powered to detect minimal clinically important difference, so results should not emphasise inferential statistics and hypothesis testing (Lancaster *et al.*, 2004, Thabane *et al.*, 2010).

The MRC framework for complex interventions recognises that it is likely that both qualitative and quantitative methods are needed to assess feasibility (Craig *et al.*, 2008b) and this was considered the case in this study as evaluation needed to answer 'what', 'how' and 'why' questions. Qualitative research is appropriate for evaluating the psychosocial aspects of care such as establishing appropriateness and acceptability and can contribute valid evidence and capture the human experience which is often not captured in experimental research (Evans, 2003). Qualitative research within a RCT can explore how interventions are implemented and the impact the RCT has on participants and their behaviours and outcomes (Paterson *et al.*, 2008). Combining qualitative and quantitative findings can increase confidence and credibility of results (Murphy *et al.*, 2014). Therefore, in this study a MMR embedded design was employed to confirm feasibility and inform on the acceptability and appropriateness of the intervention and to gain feedback on the outcome measures used. The study was sequential and key findings were integrated using a side-by-side approach (Creswell and Plano Clark, 2011). Overall, a quantitative drive was taken [QUAN(qual)] with emphasis placed on quantitative methods and results (figure 3.2).

6.4.2 Study specific considerations

As the MRC framework for complex interventions considers usual care rather than a placebo as appropriate (Craig *et al.*, 2008a), placebo acupuncture was not considered in this study. Also, currently no genuine placebo-controlled acupuncture trials exist (Appleyard *et al.*, 2014). Different types of sham acupuncture have been implemented in acupuncture trials including; shallow needling of acupuncture points, using non-penetrating needles, needling non-acupuncture points and needling acupuncture points which are not indicated for that specific condition, but none of these methods are

physiologically inert (Appleyard *et al.*, 2014) and sham acupuncture may have some level of effectiveness (Moffet, 2009). Therefore, despite lack of blinding introducing ascertainment bias, sham acupuncture, or a comparative intervention other than usual care (such as attention) was not used in this study.

Summary of methodological approach

- A MMR embedded design feasibility study was undertaken to inform a definitive trial assessing the effectiveness of acupuncture for treating PLSd.
- The study employed a usual care control.

6.5 Methods

6.5.1 Sample (inclusion / exclusion)

Participants were included in the feasibility study if they were: (1) 18 years of age or above, (2) of full cognitive ability and able to communicate in English, (3) subject to traumatic or medical amputation of a lower limb (greater than toes), (4) currently experiencing worst pain PLSd of ≥5 on an eleven point verbal rating scale i.e. moderate or severe PLSd (Jensen *et al.*, 2001). Participants were excluded if they: (1) had congenital limb absence, (2) were medically unwell as advised by medical staff at the ARU, (3) were pregnant, (4) where acupuncture is cautioned including, participants with poorly controlled epilepsy, severe haemophilia or other bleeding / clotting disorders, pacemakers (if using electro-acupuncture), or were undergoing or had recently undergone chemotherapy or bone marrow transplant, had any skin changes or removal of lymph nodes on the body, ear or scalp that would preclude the placement of acupuncture needles (British Acupuncture Council, 2010).

Generally sample size calculations are not necessary when completing a feasibility study but the sample size should be adequate to provide information about the parameters being assessed (Arain *et al.*, 2010, Thabane *et al.*, 2010). As the objectives of this study were to establish parameters for a definitive trial, not to establish effectiveness, no sample size power calculation was performed.

In the UK the median sample size per arm for feasibility /pilot studies is 30 (range 8-300) (Billingham *et al.*, 2013). Recommendations on sample size vary with Sim and Lewis (2012) recommending a total sample size of ≥ 50, Lancaster *et al.* (2004) a total sample size of ≥ 30 and Julious (2005) a minimum of 12 per group. However, even a very small sample size can provide informative data on implementation of procedure such as recruitment rate and acceptability of intervention (Hertzog, 2008). The greater the sample size, the smaller the standard error and greater the precision about the mean and variance (Julious, 2005). There are marked gains for each increase in one in a small sample size but gains become less pronounced as the sample size increases suggesting a sample size of 10 or 12 per group depending on the study design is adequate (Julious, 2005).

Given that the ARU was only a 12 bed unit which was not always at full capacity, usual length of stay was seven weeks and recruitment was estimated at 2 participants per month (so taking an estimated 10 months to recruit 20 participants) a sample size of 20 was deemed appropriate. Additionally, as the objectives of the study were to inform on procedure and acceptability this arbitrary number was considered adequate.

6.5.2 Recruitment

Participants were approached and recruited whilst they were inpatients at the ARU. Potential participants were identified by clinical staff, approached by the researcher, initially screened for intensity of PLSd ≥5/10, and provided with verbal and written information about the study (appendix 6.2). No consent was obtained at the time of initial contact and participants were advised to take up to seven days to read and reflect on the information provided before enrolling. All participants were given a minimum of 24 hours before enrolling. Participants who passed initial screening and were willing to participate underwent a final eligibility check by the researcher and signed two consent forms (one for the participant and one for the researcher) before being enrolled (appendix 6.3). Those declining to participate were asked for brief reasons.

6.5.3 Description of the intervention

The acupuncture group received usual care and a standard course of acupuncture. The control group received usual care only. Usual care included pharmacological medical intervention and daily rehabilitation including physiotherapy and occupational therapy as usually provided at the ARU. Physiotherapy could include; mirror therapy, GMI, desensitising exercises, general exercises and stretching, early walking aid and prosthetic use. Counselling was also available to amputees if required and was part of the patient care package provided at the ARU.

As the study was undertaken under the MRC framework for developing and evaluating complex interventions it aimed to evaluate an intervention which could be effective in everyday practice (Craig *et al.*, 2008b). It therefore took a pragmatic approach and did not insist on strict fidelity to a study protocol (Craig *et al.*, 2008a). However, the acupuncture protocol developed during the Delphi study was used to ensure reliability

(figure 4.7) and acupuncture practitioners were advised to use it as a guideline. Practitioners were advised to:

- Use TCM principles to treat the individual participants' underlying pathologies.
- Include the TCM principles; manage and reduce pain, move qi and blood, reduce stress and calm the mind.
- Use a combination of body and auricular acupuncture points.
- Treat the contralateral limb and possibly the ipsilateral limb.
- Include auricular acupuncture points such as Shen men, sympathetic and points corresponding to the lower limb.
- Depending on the health of the tissue and the individual participant include points around the stump.
- Mirror local and distal points by needling the opposite limb.
- Include points on the lower back (taking a segmental approach to dermatomal pain).
- Include points such as LI4+LR3, LR3, GV20, SP10.
- Try to obtain deqi and retain needles for 20-30 minutes.

Practitioners assessed and treated participants under the paradigm of TCM. Treatment could, depending on the practitioners' diagnosis and treatment plan, include electro-acupuncture or other adjunctive interventions. Although practitioners were free to use electro-acupuncture, due to feedback from interviews they were requested not to use it at first appointment (section 5.6.1). Due to consensus obtained in the Delphi study (section 4.6), all participants in the acupuncture group were allocated eight one hour acupuncture sessions (twice weekly for four weeks).

All acupuncture practitioners involved in the study were TCM trained, members of the British Acupuncture Council, had ≥ 15 years clinical experience and followed the safety guidelines in the British Acupuncture Guide to Safe Practice (British Acupuncture Council, 2010). Acupuncture needles were single-use, pre-sterilised, disposable, solid needles with pre-packed single use guide tubes when guide tubes were used.

6.5.4 Quantitative outcomes

Results of many feasibility studies have an emphasis on outcomes rather than on methodological issues (Bugge *et al.*, 2013). In this study, in keeping with feasibility studies, analysis focused on feasibility and not on statistical significance of results (Thabane *et al.*, 2010). It is advised that criteria should be set to measure the success of a feasibility study, based on the primary objectives, allowing evaluation of whether it is feasible to proceed to a main study (Thabane *et al.*, 2010). These recommendations were adhered to in this study and *a priori* criteria were set to determine success (figure 6.1). These criteria were developed through; (1) researcher awareness of the size of the ARU involved in this study and typical length of stay of amputees at this unit, (2) feedback from participants in the qualitative descriptive study about perceived acceptability of acupuncture and willingness to be involved in a trial, of which 87% indicated they would take part in a study, (3) discussion with practitioners working within the acupuncture unit involved in this study about providing the intervention, (4) feedback from participants in the qualitative descriptive study about completion of outcome measures, (5) feedback from clinical staff at the ARU involved in this study about potential participant recruitment and retention. The criteria developed by Shanyinde *et al.* (2011) for evaluating feasibility studies were used when reporting findings.

Figure 6.1 A priori criteria set to determine the success of the feasibility study

The feasibility study was deemed successful (able to proceed to a main study) if:

- Recruitment rate was ≥ 2 participants per month fitting the eligibility criteria.
- The study recruited ≥ 70% of all eligible potential participants.
- Of the participants recruited to group A ≥ 90% received their first acupuncture treatment within one week of recruitment.
- After randomisation and allocation ≥ 90% of participants received treatment as initially intended.
- Of the participants recruited to group A ≥ 80% received all eight acupuncture treatments.
- Of the participants recruited to group C ≤ 10% dropped out of the study.
- At the primary endpoint of the study outcome measures were completed by ≥ 90% of participants.
- At one month after completion of the study, outcome measures were completed by ≥ 60% of participants.
- Qualitative data identified that outcome measures were acceptable and appropriate, that questionnaires and rating scales were easy to complete and that outcome measures could be identified for use in a definitive trial.
- Qualitative data implied that acupuncture was an acceptable and effective intervention for treating PLSd with or without other secondary symptoms.
- Data were collected on the primary outcome measure (NRS) and effect size was calculated to inform a sample size calculation for a larger trial.
- Qualitative and quantitative data implied the acupuncture protocol used in the feasibility study was appropriate for use in a definitive multi-centred RCT.
- The researcher was not aware which group participants had been enrolled to 100% of the time.

Key: NRS, numerical rating scale; RCT, randomised controlled trial; Group A, acupuncture group; Group C, usual care group.

Alongside collecting feasibility specific data, data were collected on a variety of outcomes. This was done to explore participants experience of completing these outcome measures and to ascertain which outcomes would be appropriate for use in future trials. The MRC framework for developing and evaluating complex interventions recognises that using a single primary outcome measure may not make best use of the data and suggests using a variety of outcome measures to capture both intended and unintended consequences (Craig *et al.*, 2008a). Therefore, this feasibility study included a wide variety of outcome measures to allow for the identification of a range of appropriate outcomes which could be used in a definitive trial.

Recommendations from the Assessment Committee of the Neuropathic Pain Special Interest Group (NeuPSIG) and feedback from participants involved in the qualitative descriptive study (section 5.6.7) were taken into account when developing outcome measures for use in this trial. Although not all participants were anticipated to have chronic pain in the feasibility study (pain that persists beyond normal healing time) as PLSd is often a chronic condition and participants in a definitive study may include those with chronic pain, recommendations from the Initiative on Methods, Measurements, and Pain Assessment in Clinical Trials (IMMPACT-II) (Dworkin *et al.*, 2005) were also taken into consideration. NeuPSIG advises assessment of pain intensity, pain quality, treatment efficacy, psychological assessment, assessment of disability and assessment of health-related quality of life (Haanpää *et al.*, 2011). IMMPACT-II states six core outcome domains should be considered; pain, physical function, emotional function, participant ratings of improvement and satisfaction with treatment, symptoms and adverse effects and participant disposition (Dworkin *et al.*, 2005).

Participants completed outcomes 6 times in total. All outcomes (except the patient global impression of change (PGIC) which was only collected from end of week one) were collected face to face at time of enrolment and at the end of each week for the duration of the study by the researcher. The primary endpoint was at the end of the intervention (day 28). Outcome measures were also completed one month post completion of the study. Outcome measures were completed under the supervision of the researcher at baseline and week 1-4 whilst participants were inpatients at the ARU. The researcher gave participants the outcome measures and remained present on the

ward whilst they were being completed. Participants were asked to complete all outcomes as honestly as possible and that there were no 'right' or 'wrong' answers. The researcher did not engage or talk with participants whilst outcome measures were being completed. Outcome measures were posted to participants' one month post completion of the study. Data collection forms are included in appendix 6.4.

6.5.4.1 Primary outcome measure / pain intensity

Although feasibility studies do not need a primary outcome (Arain *et al.*, 2010) as one reason for conducting the feasibility study was to determine initial data for a primary outcome measure so that a sample size calculation could be performed (Lancaster *et al.*, 2004) a primary outcome was identified.

To measure pain IMMPACT-II recommends categorical rating of pain intensity (mild, moderate, severe) and / or a numerical rating scale (Dworkin *et al.*, 2005). Categorical rating of pain intensity were not used as the small number of categories in a categorical rating scale make it less sensitive and demand that a much larger change in pain is required before change shows up on the scale (Williamson and Hoggart, 2005). Numerical pain rating scales can take various forms including the visual analogue scale (VAS), numerical rating scale (NRS) and the verbal rating scale (VRS) (Dworkin *et al.*, 2005). NeuPSIG recommend either using NRS or VAS (Haanpää *et al.*, 2011). A VAS was not chosen in this study as some patients find the VAS hard to use (Lundeberg *et al.*, 2001) and as a result of this VAS usually have greater amounts of missing data and incomplete data compared to other pain rating scales (Dworkin *et al.*, 2005). In a systematic review, Hjermstad *et al.* (2011) reported poorer compliance with a VAS compared to a NRS. A VAS provides more scope for error compared to a NRS or VRS as two steps are involved, the estimate of pain by the patient and the clinicians' measure of the patients line (Lundeberg *et al.*, 2001). Hjermstad *et al.* (2011) reported that on evaluation of patient preference a NRS was the most favoured of the scales NRS, VAS and VRS in an age-mixed population. For the reasons listed above a NRS was chosen in this study. A NRS is reliable and valid (Lundeberg *et al.*, 2001, Lara-Muñoz *et al.*, 2004).

A NRS is an 11, 21 or 101 point scale where the end points are 'no pain' and 'pain as bad as it could be' (Williamson and Hoggart, 2005). An 11 point scale was chosen in this

study as it is recommended by IMPACT II and because Williamson and Hoggart (2005) report that 11 point scales may be the most popular with patients. Jensen *et al.* (1994) found that little information is lost if an 11 or 21 point scale is used instead of a 101 point scale and in practice many people treat a 101 point scale as a 11 point scale giving responses in multiples of 10. Therefore an 11 point scale was deemed appropriate. To facilitate consistency among studies IMMPACT II recommend a NRS should present the numbers 0-10 with a description at 0 of 'no pain' and a description at 10 of 'pain as bad as you can imagine'. It is advised that pain should be rated by a number which describes average pain over the last 24 hours or over the last week (Dworkin *et al.*, 2005). These recommendations were adhered to in this study and participants were asked to rate their average PLSd over the last week.

6.5.4.2 Secondary outcome measures

Secondary outcome measures included a NRS measuring 'worst' pain, the Short Form McGill Pain Questionnaire 2 (SF-MPQ-2), EuroQol-5 Dimensions (EQ-5D-5L), Hospital Anxiety and Depression Scale (HADS), Perceived Stress Scale 10 item (PSS-10), Insomnia Severity Index (ISI), Patient Global Impression of Change (PGIC).

In the qualitative descriptive study (section 5.6.4) participants often described PLSd as sudden jolts of pain. Therefore, as a NRS can also be used to record worst and / or least pain over either 24 hours or over the past week (Dworkin *et al.*, 2005, Haanpää *et al.*, 2011) worst pain over the past week was recorded as a secondary outcome measure.

The McGill Pain Questionnaire and its short form (SF-MPQ) are generic questionnaires applicable to any pain whose reliability and validity have been extensively documented (Katz and Melzack, 2011). The SF-MPQ was developed to be used in research settings where time was limited and is the most commonly used quality assessment tool in large neuropathic pain studies (Haanpää *et al.*, 2011). However, it does have limitations; it has not been validated for neuropathic pain assessment (Haanpää *et al.*, 2011) does not include several symptoms which are common in neuropathic pain and its responsiveness is limited through use of a four point rating scale (Dworkin *et al.*, 2009). The SF-MPQ-2 is a 22 item questionnaire which uses an 11 point rating scale and measures the major symptoms of both neuropathic and non-neuropathic pain (Dworkin *et al.*, 2009). It was

used in this study as it is reliable and valid for measuring diverse chronic pain (Lovejoy *et al.*, 2012) and is sensitive to change in diabetic neuropathy (Dworkin *et al.*, 2009).

Physical and emotional function combined can be measured with Health related quality of life scales (O'Connor and Dworkin, 2011). Health related quality of life scales are an important measure for neuropathic pain (Haanpää *et al.*, 2011) and studies frequently report reduced health related quality of life in people with neuropathic pain (Jensen *et al.*, 2007). The EQ-5D is recommended for use in neuropathic pain trials (Haanpää *et al.*, 2011) and several studies have found statistically significant improvement in response to treatment using the EQ-5D (O'Connor and Dworkin, 2011). Although, it has not been validated for use in neuropathic trials, responsiveness to change is equivocal, and results appear robust in trials with a large sample size or where recording large pain relief response in the active group (Haanpää *et al.*, 2011).

The EQ-5D is made up of five domains; mobility, self-care, usual activity, pain and anxiety / depression. In 2005 a Task Force was established to improve the sensitivity of the EQ-5D. The resulting EQ-5D-5L had an expanded Likert scale response options (from three to five) and this significantly increased the reliability and sensitivity of the questionnaire (EuroQol, 2014). The EQ-5D-5L was therefore used instead of the EQ-5D in this study

The HADS was developed to identify anxiety and depression in patients in non-psychiatric hospital departments but was subsequently found to be reliable in other settings and may be used as a measure of severity of mood states (Zigmond and Snaith, 1983). The HADS has been used extensively in clinical trials on different samples of patients especially those with cancer and other somatic illnesses (Bjelland *et al.*, 2002) and is reliable and valid (Zigmond and Snaith, 1983). Despite the brevity of the HADS it exhibits similar sensitivity and specificity to longer questionnaires designed to identify anxiety and depression (Bjelland *et al.*, 2002). It is responsive to change in neuropathic pain clinical trials (Haanpää *et al.*, 2011).

The HADS includes 7 depression and 7 anxiety items measuring cognitive and emotional aspects of depression and anxiety. Depression and anxiety subscales remain distinct and scores for both have distinct score cut-off points; 0-7 normal, 8-10 mild anxiety / depression, 11-14 moderate anxiety / depression, 15-21 severe anxiety / depression

(Zigmond and Snaith, 1983). The licence agreement for use of the HADS in this feasibility study is included in appendix 6.5.

The PSS is a 4, 10 or 14 item questionnaire which is designed to measure psychological stress (Cohen *et al.*, 1983). Items in the PSS are designed to record perception of how overloaded, uncontrollable and unpredictable life is and includes direct queries about current levels of stress (Cohen and Williamson, 1988). It was designed for use in community samples (Cohen and Williamson, 1988) and has been used widely in both physical and mental health studies (Cohen, 2000). Questions are not specific to any sub-population group (Cohen, 2014), it is reliable and valid and found to have acceptable psychometric properties across studies (Lee, 2012). The PSS is sensitive to the non-occurrence of events, ongoing life circumstances, stress related to events occurring to friends and family and expectations of future events (Cohen and Williamson, 1988).

The PSS-10 is recommended over the PSS-4 and PSS-14 (Cohen, 2000) and was used in this study as it has been found to have no loss of psychometric quality compared to the PSS-14 (Cohen and Williamson, 1988) and has in fact been shown to be superior (Lee, 2012) with a tighter factor structure and better internal reliability (Cohen and Williamson, 1988). The PSS-4 was not used as it is recommended for use when only a brief measure of perception of stress is required such as telephone interviews (Cohen, 2000). The PSS is not a diagnostic instrument and is designed to allow for comparison between groups only. There are no cut-off values for degrees of stress (Cohen, 2014).

Although outcomes on measures of sleep are not recommended in chronic pain clinical trials (Dworkin *et al.*, 2005) they are recommended in neuropathic pain trials (Haanpää *et al.*, 2011) and were included in this study both because the qualitative descriptive study identified that PLSd could affect sleep (section 5.6.5) and because acupuncture intervention may have positive benefits other than pain relief (Hopton *et al.*, 2010).

As any measure of sleep would only be a secondary outcome measure in a definitive trial, to avoid participant fatigue, only a brief measure was included. The ISI was designed as a brief screening measure of insomnia and as an outcome measure for use in research (Smith and Wegener, 2003). It measures perception of insomnia and degree of concerns or distress caused by insomnia and comprises of 7 items (Bastien *et al.*,

2001). It has distinct score cut off values ; 0-7 no clinically significant insomnia, 8-14 sub-threshold insomnia, 15-21 clinical insomnia moderate severity, 22-28 clinical insomnia severe severity (Bastien *et al.*, 2001). The ISI has the advantage of measuring symptoms within a two week period. It has been validated against both polysomnographic and prospective sleep diary measures (Bastien *et al.*, 2001, Smith and Wegener, 2003).

Global ratings of change scales allow participants to aggregate their experience of different components of treatment and give one measure of perception of benefit (Dworkin *et al.*, 2005). They provide a readily interpretable measure of participants' assessment of their symptoms (Dworkin *et al.*, 2005) and have high face validity (Kamper *et al.*, 2009). However, global rating of change scales require participants to recall their health status at a previous time point and also makes the presumption that participants will focus on concerns most relevant to himself / herself (Kamper *et al.*, 2009).

There is no consistency of design of global rating of change scales and no significant difference in performance in relation to responsiveness between a 7 point and 15 point scale (Kamper *et al.*, 2009). However, scales with fewer response items are less reliable and valid, and scales with too many may mean participants have difficulty attaching meaning to individual points (Kamper *et al.*, 2009). A seven point scale is recommended (Dworkin *et al.*, 2005). It is recommended that the health condition is mentioned in the question along with the anchor for the scale (in this case, when the participant was enrolled in the study) (Kamper *et al.*, 2009). Many authors recommend having 'no change' at the midpoint of the scale (Kamper *et al.*, 2009).

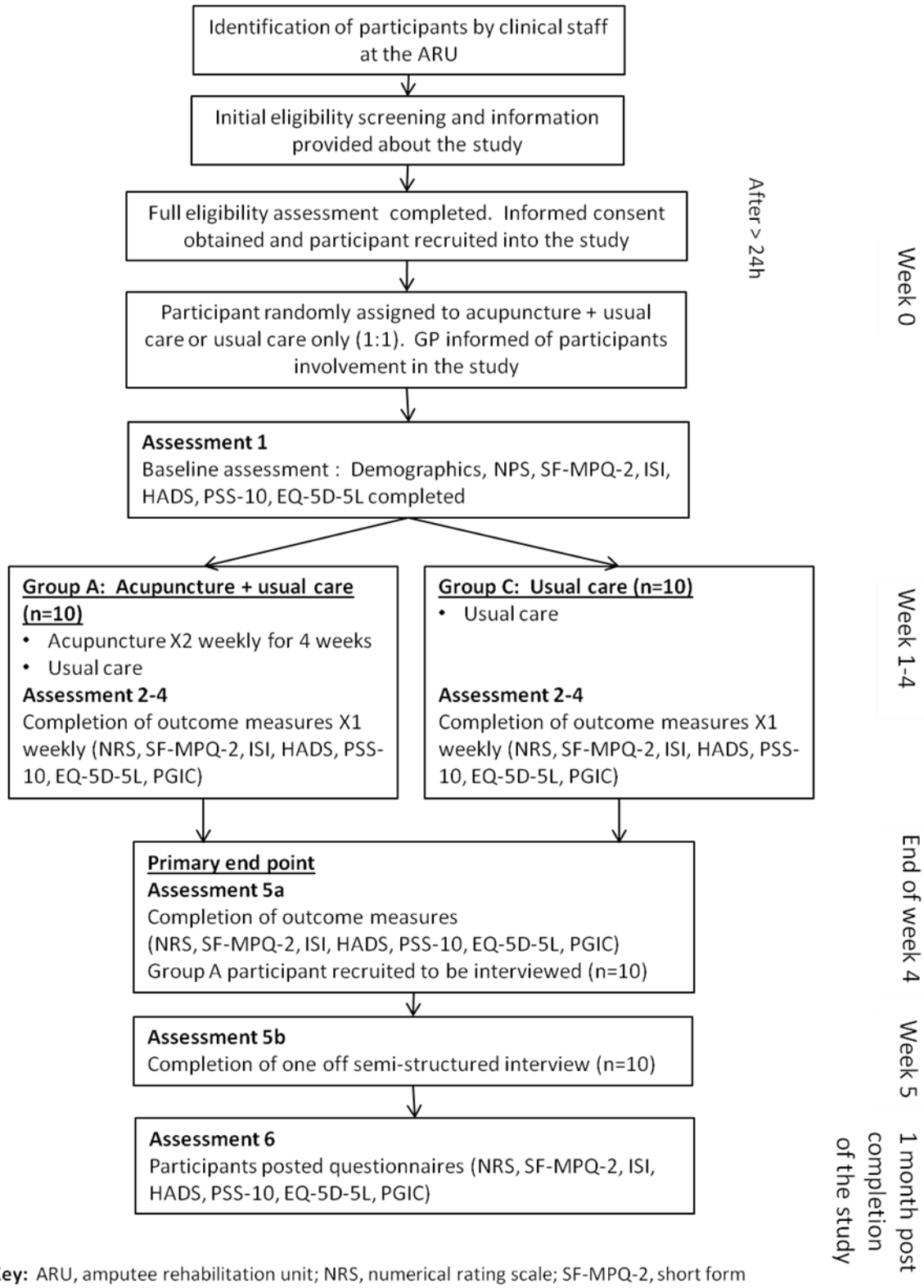
A seven point scale was used in this study, ranging from 'no change or worse' to 'a great deal better' (Hurst and Bolton, 2004). 'No change' was not at the midpoint, to allow for greater capture of positive change whilst still using a 7 point scale. Phrasing of the question was similar to the phrasing used by (Hurst and Bolton, 2004) and stated 'since being enrolled in this study, how would you describe the change (if any) in activity limitations, symptoms, emotion and overall quality of life in relation to your phantom limb pain?'

6.5.5 Interviews

Participants in the acupuncture group were interviewed post completion of the intervention. Interviews aimed to be explanatory and evaluative, understanding participants' decisions, attitudes and behaviours and factors that contributed to a successful or unsuccessful intervention. Analysis focused on the manifest content. Post completion of the RCT, the researcher requested all the acupuncture group participants (n=10) to complete a one off semi-structured interview. As qualitative research yields data which is rich in detail this arbitrary number alongside quantitative data was considered adequate to gain insight on acceptability and appropriateness of the acupuncture intervention and to gain feedback on outcome measures and other aspects of the study.

All interviews were conducted whilst participants were still inpatients at the ARU at a time convenient to the participant in a room where only the researcher and participant were present. Interviews were semi structured, facilitated by the researcher, followed a topic guide (appendix 6.6) and were audio-recorded and transcribed verbatim. All interviews commenced by asking participants about any previous experience of acupuncture, their reasons for participating in the trial and expectations towards acupuncture. Participants were then questioned about their experience of receiving acupuncture, adverse effects experienced and their experience of completing outcome measures. Field notes were made during and immediately after all interviews. Figure 6.2 shows the stages of the study.

Figure 6.2 Stages of the feasibility study



Key: ARU, amputee rehabilitation unit; NRS, numerical rating scale; SF-MPQ-2, short form McGill pain questionnaire-2; ISI, insomnia severity index; HADS, hospital anxiety and depression scale; PSS-10, perceived stress scale 10 item; PGIC, patient global impression of change.

6.5.6 Supplementary information

Supplementary information was reported on alongside outcome measures. The use of rescue medication was captured as in a future effectiveness trial this could provide important information on the efficacy of the treatment being evaluated (Dworkin *et al.*, 2005). Reporting of adverse events is essential (Dworkin *et al.*, 2005). As a minimum it is advised that passive capture of spontaneously reported events and the use of open-ended prompts should be used. Structured interviews or questionnaires are recommended to assess specific adverse events. The incidence of individual adverse events and serious adverse events should be reported on, including the percentage of participants who experienced significant adverse events. The seriousness of the adverse event should be evaluated (Dworkin *et al.*, 2005). Adverse events were captured by acupuncture practitioners through open ended prompts at each intervention point with participants. Participants were also questioned about any adverse events experienced during the trial during qualitative data collection (semi-structured interviews).

6.5.7 Withdrawals, discontinuation and post-trial care

Acupuncture is a low risk, relatively safe intervention and any adverse effects are usually temporary (section 1.3.1). In the event of mild adverse effects (drowsiness, haematoma, bleeding from a point, stuck needle, pain after needling a point) participants were not withdrawn but had the opportunity to drop out if they so wished. In the event of more serious adverse events participants were planned to be withdrawn. As acupuncture is a relatively safe treatment and this study was not assessing effectiveness, no specific arrangements were made to review interim safety and effectiveness. However, *a priori* it was planned that in the event of 3 participants reporting prolonged aggravation of pain or other serious adverse events the trial would be stopped prematurely.

To avoid concomitant care participants were asked to refrain from using other forms of complementary therapy for the duration of the trial but could receive any intervention as routinely prescribed by clinical staff at the ARU. Post completion of the study participants were free to access acupuncture through their GP / physiotherapist.

6.5.8 Randomisation, allocation concealment and blinding

As the study aimed to generate data on acceptability of randomisation, randomisation and allocation concealment were implemented. Prior to commencement of the study a researcher not involved in the study randomly allocated and concealed the allocation. A copy of the randomised sequence was kept in a locked cabinet away from the researcher. The researcher who enrolled participants and assigned them to either acupuncture intervention or the control group did not know the random sequence or treatment allocation.

Randomisation was achieved using a computer generated random numbers table and was unstratified and balanced (1:1). As simple randomisation may allocate different numbers of participants to each study group (Efird, 2011) permuted blocking was used to achieve balance between study arms. A block size of 4 was used in this study. Allocation concealment was implemented as recommended by Higgins and Altman (2008) using sequentially numbered, opaque, sealed envelopes. Envelopes were opened by the participant and the acupuncturist involved in the study only after participant details were written on the envelope. Both were requested not to inform the researcher of the participant's allocation for the duration of the study.

Sham acupuncture was not used for the reasons previously stated above (section 6.4.2) and therefore participant blinding was not possible. Practically, it was not possible to blind practitioners involved in the study. To minimise ascertainment bias in future trials, this study determined the feasibility of blinding the researcher collecting outcome measures to participants' allocation.

6.5.9 Data analysis

As this study was a feasibility study no significance tests were performed and no hypothesis testing is reported. All statistical analysis was undertaken using SPSS Version 21 software. An intention to treat approach was taken during data analysis. Intention to treat analysis can be considered as a complete trial strategy rather than solely as an approach to analysis (Gupta, 2011). It is essential in pragmatic trials (Hollis and Campbell, 1999) and ignores noncompliance, protocol deviations and withdrawals and

preserves sample size. Although there are arguments against using this approach; estimate of treatment effect is usually conservative due to dilution caused by noncompliance and interpretation of results may be difficult if there is a large cross over of participants from one treatment arm to the other, it is a recommended approach for RCTs (Gupta, 2011). Recommendations by Hollis and Campbell (1999) on intention to treat analysis were adhered to in this study; missing responses of primary outcome measures were minimised and where possible data were still collected from participants who had withdrawn from the study, all participants were analysed in the group to which they were allocated, numbers of deviations from random allocation and missing responses were provided and conclusions were based on intention to treat analysis.

In keeping with the principle of intention to treat analysis, missing data were imputed and included in analysis. For cross sectional data multiple imputation is recommended, and for longitudinal follow up last observation carried forward (LOCF) or statistical methods such as growth curve analysis (Streiner, 2002). LOCF should give conservative results as it operates against the hypothesis that people will improve over time so underestimating the degree of improvement. However, LOCF can be liberal when applied to a control group as it ignores the fact that many disorders improve over time and so may artificially inflate the difference between groups. It also underestimates negative outcomes and ignores the trajectory of data (Streiner, 2002). Although statistical methods such as growth curve analysis, random effects modelling and structured covariance matrix analysis are optimal methods of dealing with missing data, as this study was a feasibility study and was not evaluating effectiveness, and as there were insufficient data for these methods, LOCF was used. Other methods could be used in a definitive trial.

Categorical participant baseline characteristics were reported as frequencies. As the symmetry of continuous variables could not be ensured, continuous data were reported as median and quartiles (CONSORT, 2010). As this study had a small sample size it was recognised that there could be differences between the groups baseline characteristics. However, as the purpose of the study was to evaluate feasibility and not to establish the effectiveness of the intervention, and as the study was underpowered, inferential statistics were not used to compare baseline characteristics.

As normality of data could not be assumed, during descriptive analysis, data from all outcome measures were reported using median and quartile values (LAERD, 2013, Pallant, 2013). As normality of data could not be assumed confidence intervals were not calculated (Field, 2013). Effect size is an objective and standardised measure of the magnitude of an observed effect. It has the advantage of not being affected by sample size and can be compared across different studies that have used different variables or different scales of measurement (Field, 2013). It is calculated to provide information on the relative magnitude of difference (Pallant, 2013). In this study, effect size was calculated as recommended by Field (2013) using the calculation:

$$\text{Effect size} = z \div \sqrt{n}$$

> *Z indicates a standardised score expressing how many standard deviations a score is away from the mean. With data which is not normally distributed, results can be converted to a z score, allowing for comparison against a normal distribution. (Field, 2013).*

Regardless of the effect being looked for, the variables which have been measured, or how those variables have been measured, Cohen's criteria has been suggested and widely accepted to determine the size of this effect (Field, 2013 and Pallant, 2013). This criteria, as described below, was used in this study:

0.1 = small effect. The effect explains 1% of the total variance.

0.3 = medium effect. The effect accounts for 9% of the total variance.

0.5 = large effect. The effect accounts for 25% of the variance.

Using effect size data generated from this study and taking the assumption that a future study would: (1) use an 11 point NRS measuring average pain over the last week, (2) have normally distributed data, (3) use a two tailed independent samples T Test to compare acupuncture versus usual care, (4) set power and level of significance / α-level at 0.8 and 0.05 respectively, a sample size for a future definitive trial was calculated using the equation:

$$n = \frac{2(Z_a + Z_{1-\beta})^{2\sigma 2.}}{\Delta^2}$$

(Kadam and Bhalerao, 2010)

Framework analysis procedure (Ritchie and Spencer, 1994) as described in table 5.1 was used to analyse qualitative data. In brief, NVIVO 10 was used to develop the analytical framework and index transcripts. Excel was used during charting. Interviews were transcribed verbatim. Specific steps were followed during data analysis including; familiarisation, coding, identifying an analytical framework, indexing, charting and mapping / interpretation. All codes and themes were developed inductively during analysis of the data.

Inferences were drawn from separate analysis of qualitative and quantitative findings. Meta-inferences were drawn through combining key qualitative and quantitative findings. In this study feasibility specific data were presented as a side-by-side comparison as described by Creswell and Plano Clark (2011). A joint display or data transformation were not done as qualitative interviews were not conducted primarily for triangulation purposes but to gain information on the acceptability and feasibility of the trial.

6.5.10 Ethics

Ethical approval was granted from NRES Committee London – Bloomsbury in July 2014 and Guy's and St Thomas' R&D and London South Bank University in October 2014 (appendix 6.7). The trial was registered with ClinicalTrials.gov (NCT02126436). The trial aimed to commence recruitment in July 2014 but due to awaiting ethical approval, commenced in October 2014. The study end date was extended and closed in October 2015.

The study was conducted adhering to London South Bank University Code of Practice and NRES Committee London – Bloomsbury. In keeping with the principles of the Declaration of Helsinki research was only conducted by a researcher with appropriate training and qualifications, the researcher assessed the risks and burdens of the study on participants, participation was voluntary, every precaution was taken to protect the

privacy and confidentiality of participants, participants were adequately informed of the aims, methods, sources of funding, conflicts of interest, institutional affiliation of the researcher and benefits and risks associated with the study. The study was registered on a publicly accessible database before recruitment of the first subject. The researcher made results of the study publically available and adhered to accepted guidelines for ethical reporting (World Medical Association, 2008).

Information about participants was not disclosed outside the research settings. Identity of participants was kept strictly confidential. All participants were given an identification number to allow the researcher to remove names from data. Any identifiers from the interview were removed before the transcripts were used. A filing system was developed which contained the participant's identification number, outcome measures, interview and any other paperwork linked to the participant. A master list of the participant's name and identification was developed and kept separately. All hard data were kept in a locked cabinet and other data on a university password protected computer.

Summary of study methods

- A feasibility study using a MMR embedded design was undertaken.
- The study aimed to randomly assign 20 participants to either usual care or usual care plus acupuncture.
- Acupuncture was delivered pragmatically by TMC trained practitioners twice weekly for four weeks.
- Participants in the acupuncture group were interviewed post completion of their involvement in the study.
- Outcomes were collected at baseline, weekly for the duration of the study and one month post completion of the study.
- Data analysis focused on feasibility specific criteria.

6.6 Results

6.6.1 Baseline characteristics

Demographic details of participants enrolled in the study are presented in table 6.1. Median age of participants was similar across groups. In the acupuncture group, participants' median age was 50.5 years (47.0, 58.0) and in the control group 58.0 years (51.5, 66.5). There were differences in gender between groups. In the acupuncture group six were males and in the control group five were females. In both groups, participants were predominately of white British ethnicity and had varied employment status. Participants in the control group had less history of pathology than in the acupuncture group.

Across groups time since amputation was similar, with a median time in the acupuncture group of 24.5 (19.5, 29.5) days and a median time in the control group of 20.0 (16.0, 42.5) days. In the acupuncture group the majority of participants were below knee amputees, and in the control group the majority were above knee amputees. In both the acupuncture and usual care group the predominate reason for amputation was vascular pathology. Across groups history of past amputation was rare. All participants in both groups were wheelchair bound when recruited into the trial.

Median baseline scores for the primary outcome measure, average pain, were similar between groups (acupuncture group median average pain 6.3 (3.3, 7.0) control group median average pain 6.0 (3.0, 7.0)). Secondary outcome measure baseline scores were also similar between groups except for the ISI. The acupuncture group baseline median score indicated sub-threshold insomnia (a score between 8-14) but the control group indicated no clinically significant insomnia (a score between 0-7). In both the acupuncture and control group baseline HADS anxiety and depression median scores were normal (score of ≤ 7).

Note: *where median has been reported, the following numbers in brackets are the lower and upper quartiles.*

Table 6.1 Feasibility study participant demographics

Participant demographics	Acupuncture group (n=8)	Control group (n=7)
Age median (quartiles)	50.5 (47.0, 58.0)	58.0 (51.5, 66.5)
Gender n (%):		
Male	6 (75.0)	2 (28.6)
Female	2 (25.0)	5 (71.4)
Ethnicity n (%):		
White British	7 (87.5)	4 (57.1)
Black Caribbean	1 (12.5)	1 (14.3)
Black African	0 (0.0)	1 (14.3)
White other	0 (0.0)	1 (14.3)
Employment status n (%):		
Student	0 (0.0)	1 (14.3)
Unemployed	1 (12.5)	0 (0.0)
Sick leave	5 (62.5)	3 (42.9)
Retired	2 (25.0)	3 (42.9)
Time since amputation in days median (quartiles)	24.5 (19.5, 29.5)	20.0 (16.0, 42.5)
Level of amputation n (%):		
Above knee	2 (25.0)	4 (57.1)
Below knee	6 (75.0)	3 (42.9)
Reason for amputation n (%):		
Vascular	5 (62.5)	3 (42.9)
Trauma	2 (25.0)	2 (28.6)
Infection	0 (0.0)	1 (14.3)
Other	1 (12.5)	1 (14.3)
History of past amputations n (%):		
Yes	2 (25.0)	1 (14.3)
No	6 (75.0)	6 (85.7)
General health n (%):		
Diabetes I	1 (12.5)	0 (0.0)
Diabetes II	3 (37.5)	2 (28.6)
Cancer	1 (12.5)	0 (0.0)
Osteoarthritis	1 (12.5)	0 (0.0)
Epilepsy	1 (12.5)	0 (0.0)
Nil	1 (12.5)	5 (71.4)
Mobility level n (%):		
Wheelchair	8 (100.0)	7 (100.0)

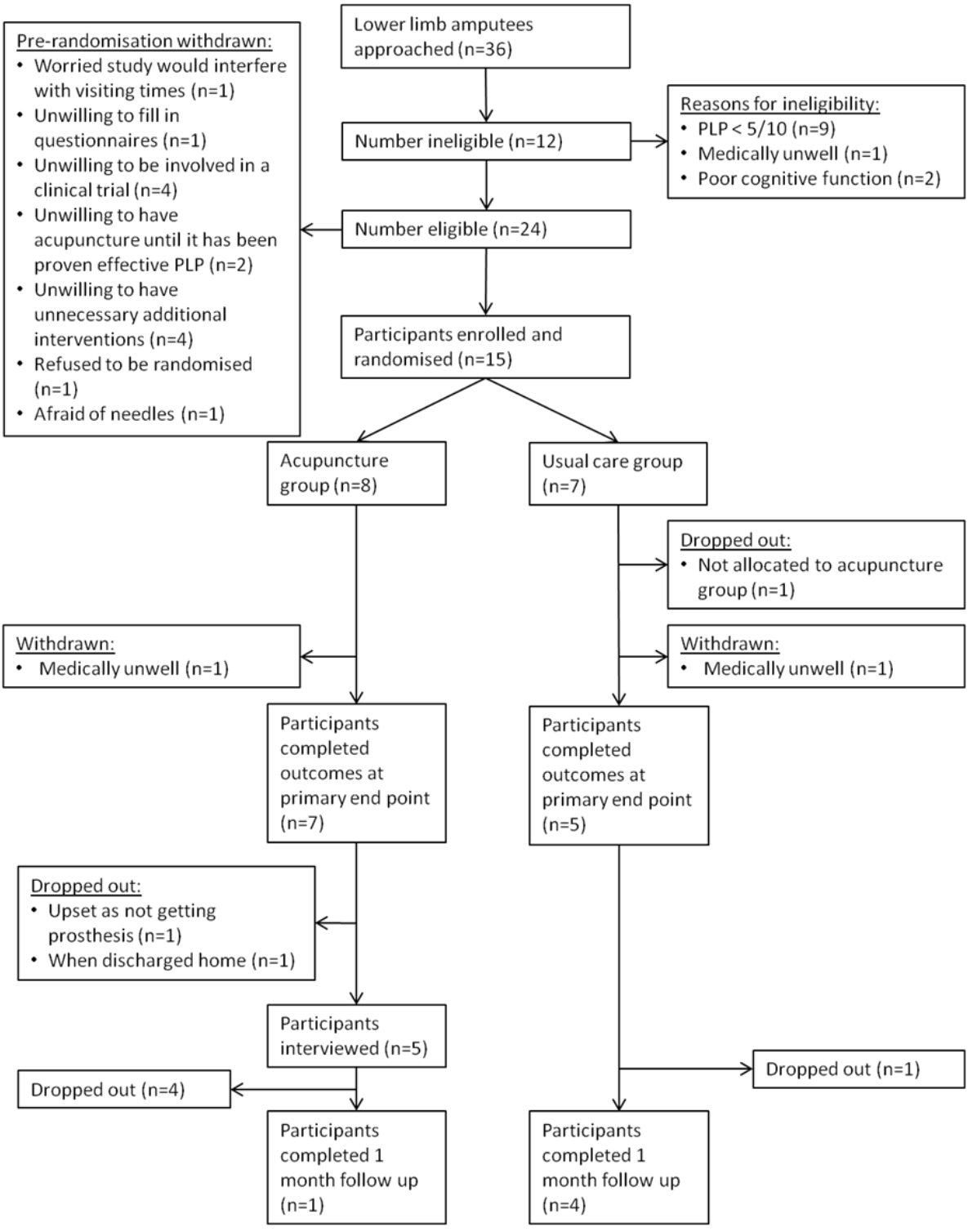
6.6.2 Eligibility, recruitment and consent

During the period 10th October 2014 to 4th September 2015 a total of 36 lower limb amputees were identified by clinical staff at the ARU and approached by the researcher. Of these 12 were ineligible for participation due to reasons including; being medically unwell (n=1), cognitively impaired (n=2), PLSd < 5/10 (n=9). Of the 24 which were eligible, 9 refused to consent to participate due to reasons presented in figure 6.3. A total of 15 participants were enrolled in the study of which 8 received acupuncture and 7 usual care.

Identification of participants proved difficult despite an extended recruitment period. Although the researcher attended the ARU weekly and discussed new patients with clinical staff (physiotherapists and doctors), potential participants were not always identified. Additionally, over the course of the trial the ARU did not always run at full capacity and some amputees were not discharged after 7 weeks, reducing the turnover of patients through the unit. Inclusion into the study required amputees to have an intensity of PLSd ≥ 5/10. This had a large impact on eligibility and 9 amputees were excluded from the study due to not meeting this criterion. Other factors which affected eligibility and recruitment into the trial were the cognitive function of amputees and medical health. Additionally, of those who were eligible and were recruited into the study two became ineligible during the course of the study due to becoming medically unwell.

A total of 24 participants were identified who were eligible to participate in the study, and of these 15 (62.5%) consented to participate. Reasons why participants did not consent are provided in figure 6.3 and include unwillingness to be involved in a clinical trial and unwillingness to receive any unnecessary additional interventions. Additionally, qualitative data identified that amputees may not have had past experience of acupuncture, were apprehensive and worried about receiving acupuncture, were sceptical and had low or no expectations of its effectiveness. Although these reasons were not identified in those refusing to consent, they may have been underlying reasons affecting recruitment.

Figure 6.3 Participant flow through the feasibility study



Note: *As some eligible amputees gave more than one reason for not participating in the trial, a total of 14 reasons for pre-randomisation withdrawal were given by nine lower limb amputees.*

6.6.3 Randomisation and blinding procedure

The process of randomisation described in section 6.5.8 worked smoothly. However, due to the small sample size, between groups there were differences in baseline demographics (section 6.6.1). Randomisation was generally considered acceptable with only one potential participant refusing to be randomised and one participant dropping out due to being randomised into the control group. All enrolled participants received treatment as allocated. Qualitative data suggested randomisation was acceptable with interviewees being willing to be randomised to either the acupuncture or usual care group. Blinding however was not successful. Participants and clinical staff at the ARU unintentionally informed the researcher of the participants' group allocation.

6.6.4 Acceptability of the intervention

Participating in the study was not initially perceived as acceptable by some participants and 37.5% eligible participants refused to participate. Qualitative findings suggested that on being informed about the study amputees did not always consider acupuncture positively, were worried and apprehensive about acupuncture and about being enrolled into the study. Once enrolled, no participants in the acupuncture group, and only one in the control group dropped out before the primary end point of the study, suggesting both the acupuncture protocol and usual care control were acceptable.

Qualitative data suggested that the acupuncture protocol was acceptable to participants. Although participants generally did not like the physical process of being needled, the intervention was perceived to be relaxing and participants generally looked forward to treatment. Electro-acupuncture was considered a pleasant experience. Generally receiving two treatments a week was considered acceptable, but could be considered too much if physiotherapy / occupational therapy sessions were tiring. However, having acupuncture when tired was also perceived to be beneficial. Acupuncture sessions needed to be spaced out evenly through the week to be acceptable.

In keeping with the holistic nature of TCM acupuncture, the intervention was perceived to be beneficial for treating both PLSd and other ailments. Generally a couple of sessions

were needed before a benefit was felt and symptoms could get worse before they got better. Overall, the acupuncture protocol was considered acceptable, good and beneficial for treating PLSd. Resolving PLSd had the additional benefit of improving wellbeing. One participant reported being calmer and not worrying, another reported not feeling annoyed about PLSd, and another reported feeling less stressed and sleeping better. Supporting this qualitative data, quantitatively, average pain decreased more in the acupuncture group than in the control group during the study. In the acupuncture group median pain scores decreased from 6.3 (3.3, 7.0) to 1.5 (0.3, 6.3) and in the control group scores decreased from 6.0 (3.0, 7.0) to 4.0 (2.0, 7.0). Median worst pain also decreased to a greater extent in the acupuncture group compared to the control. In the acupuncture group median worst pain scores decreased from 8.5 (5.5, 10.0) to 2.5 (0.0, 8.8) and in the control group from 8.0 (7.0, 8.0) to 6.0 (4.0, 8.0).

6.6.4.1 Adverse effects

No data were collected by the acupuncture practitioner on adverse events. Qualitative data identified that when asked four of the participants interviewed did not perceive the intervention to cause adverse effects. However, during the course of the interviews two participants spontaneously reported some bleeding from some points during the removal of needles, one reported some pain during auricular acupuncture and bleeding and itching after and one reported one episode of pain when the electro-acupuncture machine was turned up too high. One participant reported adverse effects from electro-acupuncture. Electro-acupuncture reproduced pre-amputation pain once, caused one episode of bruising and flared up PLSd for a couple of hours post treatment.

6.6.5 Retention and compliance / adherence

Participant retention was good during the intervention and up to the primary endpoint of the study. Before the primary end point of the study only two participants were withdrawn from the study due to being medically unwell and one dropped out due to being randomised to the control group. However, participant retention post completion of the intervention was poor. A total of 10 participants did not complete the one month follow up questionnaire and 2 participants refused to be interviewed. The two who refused to be interviewed did so because one discovered he was not getting a prosthetic

limb and was upset about this, and the other because he was about to be discharged home and did not want further involvement in the study. This participant was offered a home telephone interview but refused to partake.

Participant adherence to the acupuncture protocol was good. Although no participants received all eight acupuncture treatments, only four were missed due to poor participant compliance. Reasons given were due to; tiredness, forgetting appointments, appointments coinciding with another medical appointment, not wanting further treatment as PLSd had resolved. Two treatments were also missed because a participant was discharged early. Qualitatively, factors which could affect adherence in a definitive trial were identified. Acupuncture appointments sometimes coincided with other medical appointments and needed to be rescheduled. One participant frequently forgot her acupuncture appointments as they were not written on her daily timetable.

Although participant adherence to the acupuncture protocol was good, the acupuncture practitioner did not fully comply with the protocol. Treatment was only offered twice weekly for the duration of the study to two participants. The practitioner did not document why treatment was often only offered once weekly to the remaining participants. Median total number of treatments received was 5.0 (4.0, 6.0). Despite the protocol advising using a combination of auricular and body acupuncture this was only given to one participant on two occasions. Both lower limbs were treated 66.7% of the time whereas the contralateral limb only was treated only 8.3% of the time. Local and distal points were used as recommended in the protocol and a segmental approach to dermatomal pain was taken when treating 1 participant (table 6.2). Although points such as LR3, GV20 and SP10 were used as advised in the protocol, these were not the most frequently used points (appendix 6.8). Needle retention time was not recorded. In keeping with the study protocol, the practitioner took a pragmatic approach to treatment and treated participants underlying pathologies alongside PLSd.

Table 6.2 Treatment approach taken by acupuncture practitioners during the feasibility study

Limb / area treated	Frequency treated
Residual limb only	0
Contralateral limb only	3
Both lower limbs	24
Lumbar area only	2
Lumbar area + contralateral limb	3
Upper limb only	2
Upper limb + residual limb	1
Upper limb + residual limb + contralateral limb	1
Auricular points	2
Other points (yintang, LI4, GV20)	2
Treating other areas (shoulder, ankle, thoracic area)	10

6.6.6 Outcome assessment

Adherence to completing the outcome measures were good both for both the control and acupuncture group, and all those enrolled in the study completed all outcomes weekly up until the primary end point of the study. Adherence to completing outcome measures at one month follow up, however, was poor with only one participant in the acupuncture group and four in the control group completing and returning outcome measures. Qualitative data found that completing outcome measures weekly up until the primary end point of the study was acceptable. Outcome measures were generally perceived as easy to complete. They were considered to capture the full experience of PLSd and completing them was perceived to be beneficial. Participants found completing them made them think about their health and how it had changed. There was also the view that it was something to do and participants liked 'chatting to the researcher'. Participants generally considered the length of time to complete the questionnaires and frequency of completing them was acceptable.

Despite the researcher's attempt to obtain information on the use of rescue medication, this was not possible as participants were often unsure of their medication and changes to their medication. The researcher did not have access to participants' medical records. Adverse events from acupuncture were captured during semi-structured interviews, but were not recorded by the acupuncture practitioner.

6.6.7 Selection of most appropriate outcomes

All outcomes were completed fully. However, quantitative findings suggested that the HADS, PSS-10 and EQ-5D-5L outcome measure may not be appropriate for use in a definitive trial. With the HADS even at baseline, participants in both the acupuncture and control group had normal anxiety and depression scores, implying that anxiety and depression levels may be normal in this demographic group. The PSS-10 and EQ-5D-5L did not capture change. The ISI may not be appropriate in an inpatient unit as anecdotally participants reported that factors other than PLSd affect sleep, such as noise and medication. Qualitative data suggested that the SF-MPQ-2 may include some terminology which participants do not understand. Although not captured during interviews, the researcher noted that participants had trouble understanding the wording of the PGIC suggesting this outcome may be more appropriate if worded differently and structured to allow for capture of both positive and negative change.

6.6.8 Sample size calculation

A sample size for a main trial was calculated based on data obtained from this study. Assuming a future study's power and level of significance / α-level is 0.8 and 0.05 respectively and a two tailed independent samples T Test is used to compare two groups, a sample size of 71 per group (142 in total) would be needed. According to the findings from this feasibility study, the follow up rate at 4 weeks was 80%. Therefore, considering a 20% drop-out rate, 170 participants (85 per group) are recommended to be recruited to detect a significant change in a two armed, parallel group RCT comparing acupuncture and usual care as measured using an 11 point NRS measuring average pain at four weeks.

6.6.9 All components of the protocol work together

Overall the study worked well and qualitative data suggested participants were satisfied with the study protocol. Participants generally found being involved in the study was a good experience which exceeded expectations and provided additional benefit to usual care. Qualitatively, participants' views on acupuncture changed over the course of the study. Despite participants generally being initially worried and anxious about acupuncture, by the end of the study all participants said they would recommend acupuncture to others and one participant had already recommended participating in the study to other amputees in the unit. Participants understood the information sheets and were willing to be randomised. The process of randomisation and allocation concealment was successful. The acupuncture protocol and outcome measures were considered acceptable by participants. Using the criteria set *a priori,* as shown in table 6.3, this study was found to be successful in relation to participants receiving the intended intervention, outcome measures being considered acceptable and appropriate and being completed at the primary end point of the study and the intervention being considered acceptable and appropriate for use in a definitive trial. The study was unsuccessful in relation to recruitment, practitioner adherence to the protocol, completion of outcome measures at one month follow up and blinding.

Qualitatively, factors were identified which affected treatment. These factors should be considered when developing a protocol for a definitive trial. The place where the acupuncture was given was considered to affect treatment and treatment was considered more relaxing when given in a quiet and calm environment. Acupuncture practitioner characteristics, such as being calm, attentive, gentle and professional were considered to contribute to the effectiveness of treatment. The importance of participants being in the 'right place' for treatment was identified and personal mental state was considered to affect treatment outcome. Prosthesis use affected PLSd and could both aggravate and ease symptoms.

Findings are summarised using Shanyinde *et al.* (2011) criteria in table 6.4. Outcome measure data and themes developed during qualitative data analysis are presented in table 6.5 and figure 6.4.

Table 6.3 Success of the feasibility study

A priori **criteria**	**Findings**	**Objective met (yes / no)**
Recruitment rate was ≥ 2 participants per month fitting the eligibility criteria.	Recruitment rate was 1.36 eligible participants per month.	No
The study recruited ≥ 70% of all eligible potential participants.	62.50% of all eligible participants were recruited.	No
Of the participants recruited to group A ≥ 90% received their first acupuncture treatment within one week of recruitment.	All participants received their first acupuncture treatment within a week of recruitment.	Yes
After randomisation and allocation ≥ 90% of participants received treatment as initially intended.	All participants received treatment as intended and the study protocol was considered acceptable.	Yes
Of the participants recruited to group A ≥ 80% received all eight acupuncture treatments.	No participants received all 8 treatments (median total number of treatments 5.00 (4.00, 6.00).	No
Of the participants recruited to group C ≤ 10% dropped out of the study.	One participant (14.29%) of participants dropped out of the control group.	No
At the primary endpoint of the study outcome measures were completed by ≥ 90% of participants.	100% of participants still enrolled on the study completed all outcome measures at the primary endpoint of the study.	Yes
At one month after completion of the study, outcome measures were completed by ≥ 60% of participants.	Outcome measures were completed by 5 participants (33.33%)	No
Qualitative data identified that outcome measures were acceptable and appropriate, that questionnaires and rating scales were easy to complete and that outcome measures could be identified for use in a definitive trial.	Outcome measures were considered acceptable, appropriate and easy to complete. The HADS, PSS-10, EQ-5D-5L and ISI may not be appropriate for use in a definitive trial.	Yes
Qualitative data implied that acupuncture was an acceptable and effective intervention for treating PLSd with or without other secondary symptoms.	Acupuncture / electro-acupuncture was considered acceptable. Acupuncture was perceived to be effective at treating both PLSd and other secondary complaints.	Yes
Data were collected on the primary outcome measure (NRS) and effect size was calculated to inform a sample size calculation for a larger trial.	Considering a 20% dropout rate, 170 participants are recommended to be recruited to detect a significant change in a two armed parallel RCT comparing usual care and acupuncture as measured using an 11 point NRS measuring average pain at four weeks.	Yes
Qualitative and quantitative data implied the acupuncture protocol used in the feasibility study was appropriate for use in a definitive multi-centred RCT.	Participants did not drop out of the acupuncture group suggesting it was acceptable. Participants symptoms generally improved over 6 treatments suggesting 8 treatments was adequate. Acupuncture and EA were considered acceptable, effective and relaxing.	Yes
The researcher was not aware which group participants had been enrolled to 100% of the time.	Blinding was not successful and the researcher knew through both participants and clinical staff at the ARU their group allocation.	No

Table 6.4 Evaluation of the feasibility study using Shanyinde et al. (2011) criteria

Methodological issue	Findings	Quantitative evidence	Qualitative evidence
Sample size calculation	Achieved.	Allowing for a dropout rate of 20%, 170 participants (85 per arm) would need to be recruited in a definitive trial.	
Eligibility	Ineligibility for inclusion in the study was mainly due to PLSd intensity being < 5/10.	12 out of 36 approached were ineligible.	
Recruitment	Recruitment was difficult.	Clinicians failed to identify participants. The unit was not always running at full capacity. Study end date was extended.	Participants were worried, anxious and sceptical about participating in the study and had low / no expectations of acupuncture's effectiveness.
Consent	Conversion to consent did not meet the criterion set *a priori*.	Of those eligible 62.5% consented to participate.	Participants were apprehensive and worried about acupuncture and sceptical about its effectiveness. Despite this, participants decided to participate in the trial, but hoped they would be randomised to the control group.
Randomisation procedure	Worked well.	One participant refused to consent to be randomised. One participant dropped-out due to being randomised to the control group.	Participants did not recommend changes to the study protocol and were willing to be randomised to either the acupuncture or control group.

Methodological issue	Findings	Quantitative evidence	Qualitative evidence
Blinding procedure	Unsuccessful.	The researcher was aware which group participants were allocated into.	
Compliance / adherence to intervention	Good participant adherence to acupuncture protocol. Poor practitioner adherence to protocol.	A total of 5 treatments were missed due to poor participant compliance. No participants received all 8 treatments. Only 2 participants were offered treatment twice weekly throughout the duration of the study. A combination of auricular and body acupuncture was only used on one participant.	Deviation from the protocol due to; tiredness, forgetting the appointment, the appointment coinciding with another medical appointment, not wanting further treatment as PLSd had resolved.
Acceptability of intervention	Difficulty recruiting suggested the intervention was not perceived acceptable prior to the study. Once enrolled on the study the intervention was perceived acceptable.	Of those eligible, 62.5% agreed to participate. In the control group 1 participant dropped out before the primary end point. In the acupuncture group no participants dropped out before the primary end point.	Acupuncture was considered acceptable and relaxing. Acupuncture was perceived to be effective. Electro-acupuncture was perceived to be beneficial and good. PLSd often resolved after approximately 6 treatments. Acupuncture did not cause serious adverse effects. Two treatments a week for 8 weeks was considered acceptable.

Methodological issue	Findings	Quantitative evidence	Qualitative evidence
Cost and duration of intervention	Cost not assessed. Study end date was extended.	Not evaluated.	Not evaluated.
Outcome assessment	Adherence to completing outcome measures was good up until discharge from the ARU.	All OM were completed up to the primary end point of the study. Only 5 OM were completed at one month follow up. 2 participants refused to be interviewed.	OM were considered easy. Completing OM was generally perceived to be beneficial. OM provided occupation. Length of time to complete OM and frequency of completing OM was generally considered acceptable.
Selection of most appropriate outcomes	HADS, PSS-10, EQ-5D-5L and ISI may not be appropriate in future studies. PGIC may need re-wording. Future OMs could capture amputees' perception of themselves.	Baseline HADS scores were normal (score ≤ 7). Little change was found in the PSS-10 and EQ-5D-5L scores over the duration of the study. Participants required PGIC to be explained.	Anecdotally noise and medication affected sleep. EQ-5D-5L was considered restrictive due to lack of choice of mobility levels. SF-MPQ-2 wording was not always understood by participants. One participant advised capturing data on perception of self and one on aggravating factors and timing of PLSd.

Methodological issue	Findings	Quantitative evidence	Qualitative evidence
Retention	Once recruited retention was good up until the primary end point of the study.	In the control group 1 participant dropped out before the primary end point. In the acupuncture group no participants dropped out before the primary end point. In the control group 3 participants did not complete the 1 month follow up OMs. In the acupuncture group 7 participants did not complete the 1 month follow up OMs.	Being enrolled on the study was perceived as a good experience which exceeded expectations. Even if not perceived as effective, being enrolled on the study was considered interesting. Acupuncture was considered acceptable and beneficial. One participant recommended the study to others.
Logistics of multi-centre trial	Not assessed.	Not evaluated.	Not evaluated.
All components of the protocol work together	Components worked well together. Difficulties were identified with recruitment, practitioner adherence to the protocol, completion of OM at one month follow up and blinding.	No difficulties were identified in randomisation, allocation concealment, participants receiving the intended intervention, participant progress through the study, outcome measures being completed at the primary end point of the study. Difficulties were identified with recruitment, practitioner adherence to the protocol, completion OM at one month follow up and blinding.	Generally changes were not recommended by participants to the study protocol. One participant advised; changing the EA machines, ensuring acupuncture appointments were at an appropriate time, completing OM once monthly only, addressing amputees' acceptance of body image before treating PLSd.

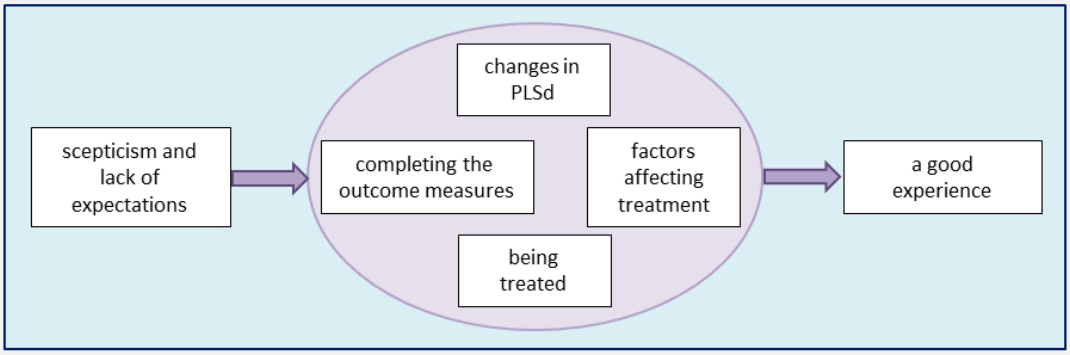
Key: OM, outcome measures; PLSd, phantom limb syndrome; ARU, amputee rehabilitation unit; EA, electro-acupuncture

Table 6.5 Feasibility study outcome measure data

	Baseline median (quartiles)	Baseline between group effect size	Day 7 median (quartiles)	Day 7 between group effect size	Day 14 median (quartiles)	Day 14 between group effect size	Day 21 median (quartiles)	Day 21 between group effect size	Day 28 median (quartiles)	Day 28 between group effect size
NRS average pain	A: 6.3 (3.3, 7.0) C: 6.0 (3.0, 7.0)	0	A: 5.5 (3.0, 7.0) C: 5.0 (3.0, 7.0)	0.0	A: 2.0 (2.0, 5.5) C: 6.0 (3.0, 7.0)	0.5	A: 3.3 (1.0, 6.8) C: 5.0 (2.0, 7.0)	0.3	A: 1.5 (0.3, 6.3) C: 4.0 (2.0, 7.0)	0.4
NRS worst pain	A: 8.5 (5.5, 10.0) C: 8.0 (7.0, 8.0)	0.2	A: 7.5 (6.3, 10.0) C: 7.0 (6.0, 8.0)	0.2	A: 5.5 (2.0, 8.8) C: 7.0 (4.0, 8.0)	0.1	A: 6.5 (1.0, 9.0) C: 7.0 (4.0, 8.0)	0.1	A: 2.5 (0.0, 8.8) C: 6.0 (4.0, 8.0)	0.3
SF-MPQ-2	A: 2.9 (1.7, 3.4) C: 2.4 (2.0, 3.3)	0.1	A: 2.4 (1.2, 3.6) C: 2.4 (1.3, 2.5)	0.1	A: 0.7 (0.5, 2.9) C: 1.2 (0.9 3.6)	0.4	A: 0.9 (0.3, 2.5) C: 1.2 (0.9 2.4)	0.3	A: 0.5 (0.0, 2.6) C: 1.2 (0.6, 2.4)	0.3
HADS anxiety	A: 6.5 (2.3, 10.3) C: 5.0 (3.0, 8.0)	0.1	A: 6.0 (0.3, 11.0) C: 4.0 (3.0, 7.0)	0.0	A: 5.5 (0.5, 8.0) C: 3.0 (2.0, 8.0)	0.0	A: 6.0 (2.0, 7.8) C: 4.0 (1.0, 7.0)	0.2	A: 5.0 (1.3, 9.5) C: 3.0 (1.0, 9.0)	0.1
HADS depression	A: 6.0 (3.3, 9.0) C: 4.0 (2.0, 7.0)	0.2	A: 5.0 (3.3, 8.3) C: 4.0 (3.0, 7.0)	0.1	A: 5.5 (2.3, 8.5) C: 4.0 (2.0, 7.0)	0.1	A: 5.5 (2.5, 8.5) C: 3.0 (2.0, 7.0)	0.2	A: 5.0 (1.0, 10.5) C: 4.0 (2.0, 7.0)	0.0
PSS-10	A: 16.0 (11.3, 18.0) C: 18.0 (10.0, 19.0)	0.2	A: 13.5 (6.5, 17.8) C: 15.0 (10.0, 18.0)	0.2	A: 13.5 (7.3, 17.8) C: 16.0 (10.0, 19.0)	0.2	A: 18.0 (6.5, 22.0) C: 12.0 (9.0, 20.0)	0.0	A: 10.0 (6.3, 18.0) C: 16.0 (9.0, 19.0)	0.2
ISI	A: 12.5 (6.5, 21.0) C: 4.0 (2.0, 18.0)	0.2	A: 12.0 (4.0, 19.3) C: 6.0 (2.0, 16.0)	0.3	A: 11.0 (3.5, 17.4) C: 11.0 (2.0, 15.0)	0.2	A: 9.5 (3.5, 19.5) C: 7.0 (0.0, 15.0)	0.2	A: 6.5 (1.3, 16.8) C: 9.0 (0.0, 15.0)	0.2

	Baseline median (quartiles)	Baseline between group effect size	Day 7 median (quartiles)	Day 7 between group effect size	Day 14 median (quartiles)	Day 14 between group effect size	Day 21 median (quartiles)	Day 21 between group effect size	Day 28 median (quartiles)	Day 28 between group effect size
EQ-5D-5L mobility	A: 5.0 (5.0, 5.0) C: 5.0 (5.0, 5.0)	0.2	A: 5.0 (5.0, 5.0) C: 5.0 (5.0, 5.0)	0.0	A: 4.5 (3.0, 5.0) C: 5.0 (4.0, 5.0)	0.2	A: 4.5 (3.0, 5.0) C: 5.0 (3.0, 5.0)	0.1	A: 4.0 (3.0, 4.8) C: 5.0 (3.0, 5.0)	0.3
EQ-5D-5L self care	A: 2.0 (1.0, 2.0) C: 1.0 (1.0, 2.0)	0.2	A: 1.5 (1.0, 3.0) C: 1.0 (1.0, 2.0)	0.2	A: 1.5 (1.0, 3.0) C: 1.0 (1.0, 2.0)	0.2	A: 1.5 (1.0, 2.0) C: 1.0 (1.0, 2.0)	0.1	A: 1.5 (1.0, 2.0) C: 2.0 (1.0, 2.0)	0.0
EQ-5D-5L usual activities	A: 4.0 (2.3, 5.0) C: 5.0 (4.0, 5.0)	0.2	A: 4.0 (2.5, 5.0) C: 4.0 (3.0, 5.0)	0.1	A: 3.0 (2.0, 4.0) C: 4.0 (2.0, 5.0)	0.3	A: 3.0 (2.0, 3.8) C: 4.0 (3.0, 5.0)	0.4	A: 3.0 (2.0, 3.8) C: 4.0 (3.0, 5.0)	0.4
EQ-5D-5L pain / discomfort	A: 4.0 (3.0, 4.0) C: 3.0 (2.0, 3.0)	0.6	A: 3.0 (3.0, 3.8) C: 3.0 (2.0, 3.0)	0.4	A: 4.0 (2.3, 4.8) C: 3.0 (3.0, 3.0)	0.4	A: 3.0 (2.0, 3.8) C: 3.0 (2.0, 3.0)	0.2	A: 3.0 (2.0, 3.8) C: 3.0 (2.0, 3.0)	0.2
EQ-5D-5L anxiety / depression	A: 2.0 (1.0, 2.8) C: 1.0 (1.0, 2.0)	0.2	A: 2.0 (1.3, 2.8) C: 2.0 (1.0, 2.0)	0.2	A: 1.5 (1.0, 3.0) C: 2.0 (1.0, 2.0)	0.1	A: 1.5 (1.0, 3.0) C: 1.0 (1.0, 2.0)	0.2	A: 2.0 (1.0, 3.0) C: 1.0 (1.0, 2.0)	0.2
EQ-5D-5L health today	A: 62.5 (50.0, 82.5) C: 75.0 (50.0, 80.0)	0.1	A: 85.0 (65.0, 88.8) C: 80.0 (70.0, 80.0)	0.3	A: 75.0 (60.0, 90.0) C: 70.0 (50.0, 80.0)	0.1	A: 82.5 (63.8, 88.8) C: 80.0 (55.0, 85.0)	0.2	A: 77.5 (60.0, 90.0) C: 80.0 (75.0, 90.0)	0.0
PGIC			A: 3.0 (1.0, 5.0) C: 1.0 (1.0, 6.0)	0.0	A: 5.0 (5.0, 6.0) C: 3.0 (1.0, 5.0)	0.5	A: 5.0 (4.0, 7.0) C: 4.0 (2.0, 6.0)	0.3	A: 6.0 (4.0, 7.0) C: 3.0 (1.0, 5.5)	0.5

Figure 6.4 Key themes identified during qualitative data analysis of feasibility study interviews



Theme	Quote
Scepticism and lack of expectations	"I was a bit worried about what it was all about. You said acupuncture and I said I'm not keen on that. And then I thought I'll try it I'll try it out."(Interview 1) "Didn't expect it to work. Very, very very sceptical me, very. That's how ignorant I was…. I didn't think it would work, I thought it was all nonsense."(Interview 4)
Being treated	"it was so relaxing…. and um I was just lying there and I could have quite easily gone to sleep! It was so relaxing, so sort of peaceful"(Interview 2)
Changes in phantom limb pain	" I said well, it's good. It's very good….. It works good and then last time she came she said aren't you going to have it? I said no, no, it's got rid of that pain that was down there."(Interview 1)
Factors affecting treatment	"She [the acupuncturist] looked after you well and I think that was a lot of it, her personality and the way she treated you and everything."(Interview 2) "I think because of the environment it was being done in and the timing more than anything, I think it wasn't really a positive thing. It might have been a different story in another setting, if I had more time around my schedule"(Interview 3)
Completing the outcome measures	"[SF-MPQ-2] A couple of the wordings were a bit weird. I didn't get some of the words on the describe the pain, gruelling and what was the other one, there were a couple of them I didn't understand what these words meant."(Interview 4)
A good experience	"it's been very positive…. it's been an extra benefit I would definitely say that…. I couldn't criticise anything to be perfectly honest."(Interview 5)

Summary of results

- Eligibility was affected by setting an inclusion criterion of PLSd ≥5/10.
- Recruitment was affected by lack of identification of all potential participants and lack of willingness of those identified to be enrolled.
- Blinding of the researcher was unsuccessful.
- The acupuncture protocol and a usual care control were acceptable.
- Participant compliance was good until discharge from the ARU.
- Practitioner compliance with the protocol was poor in terms of frequency and total number of treatments provided, the use of auricular acupuncture and the use of points taking a segmental approach to dermatomal pain.
- The HADS, PSS-10 and EQ-5D-5L may not be an appropriate outcome measure in this demographic group.
- The ISI may not be appropriate in an in-patient setting.
- Obtaining data on rescue medication is difficult in an inpatient setting where patients do not self-medicate.
- The acupuncture practitioner did not report on adverse events.
- Assuming a future study had two independent groups, used the independent samples T Test during analysis, and allowed for a 20% dropout rate, a sample size of 85 participants per group would be needed in a future definitive trial.

6.7 Discussion

The feasibility study met its objectives and provided useful information which could inform the design of future studies despite recruiting only a small number of participants.

6.7.1 Baseline characteristics

As this study had a small sample size it was recognised that there could be differences between the groups baseline characteristics. However, as the purpose of the study was to evaluate feasibility and not to establish the effectiveness of the intervention this was not seen as a limitation of the study. However, imbalances between baseline group variables would need to be considered when undertaking a definitive trial as imbalances can influence outcomes and cause chance bias (Roberts and Torgerson, 1999). A future definitive study should ensure adequate sample size and that randomisation has been properly conducted. If this is done, as all groups should have come from the same population, there should not be significant differences between the groups' baseline characteristics (Roberts and Torgerson, 1999).

6.7.2 Eligibility, recruitment and consent

Recruitment of participants was problematic and the study did not meet its target of recruiting ≥ 2 participants per month or 20 participants in total. This is not unusual and other studies have also reported recruitment as being slower or more difficult than expected. A study by McDonald *et al.* (2006) identified that only 31% of trials successfully recruited 100% of their target. A total of 34% revised their target, 54% required an extension and 45% recruited new centres to ensure delivery. Recruitment has been deemed problematic due to fewer eligible participants than expected being identified, internal problems, participants not being willing to participate and eligible participants being missed (McDonald *et al.*, 2006). Recruitment can be affected at different levels including; the patient, the recruiter, the trial centre, the trial organisation and the trial design (Fletcher *et al.*, 2012). Communication can affect recruitment (Paramasivan *et al.*, 2011) and maintaining recruitment activity over time can be problematic as enthusiasm for the study dies (Fletcher *et al.*, 2012). This study

required an extension due to the delayed start date and experienced similar problems to recruitment as identified by McDonald *et al.* (2006). Recruitment was considered to be affected as the patient group was unwilling to undergo unnecessary interventions or be involved in a clinical trial, the trial centre did not always identify potential participants and the intervention was perceived negatively by some amputees. It has been suggested that clinical staff have limited time to undertake research activities (Adams *et al.*, 2015) and this may have influenced the identification of potential participants. Adequate understanding and ability to communicate details about a RCT is a key aspect of recruitment (Fletcher *et al.*, 2012) but this was not considered to be a problem in this study as the researcher providing details of the study had adequate information and qualitative data did not identify that communication about the study was inadequate. A future definitive trial would need to ensure potential participants had some education about the intervention as a brief introduction by clinical staff about acupuncture may make participants less sceptical of the intervention and more willing to consent. However, this may also then affect acceptability of being randomised to a usual care control. Future trial centres would need to ensure that adequate time and personnel were allocated to the trial and that recruiters had adequate understanding of the study and good communication skills. Although not possible in this study as this study relied on the unique co-location of an acupuncture department within an amputee rehabilitation unit, recruitment could be enhanced by a multi-centred approach.

The study identified that intensity of PLSd was a major barrier to recruitment, and many participants did not meet the inclusion criteria of PLSd ≥5/10 intensity. This was unexpected, as during the qualitative descriptive study described in chapter 5, participants often had a high intensity of PLSd. The feasibility study may not have matched what was found in the qualitative descriptive study as the qualitative descriptive findings were neither generalisable nor time or context free. Also, although as reported in section 1.2.1 PLSd can be severe, this may only be in approximately 30% of those with PLSd (Davidson *et al.*, 2010, Ehde *et al.*, 2000) explaining why including this inclusion criterion did exclude 9 potential participants. To aid recruitment, future studies may consider lowering or excluding this inclusion criterion.

The study did not meet its target of recruiting ≥ 70% of all eligible potential participants.

However, this criterion was unrealistically high and 62.5% of all eligible potential participants were recruited. Additionally, of the 36 amputees who were approached, 42% participated in the study. Other CAM studies report a lower participation rate (Hondras, *et al.,* 2008) and studies evaluating the effectiveness of interventions for treating PLSd also report a low participation rate. A RCT evaluating the effectiveness of amitriptyline for treating PLP or residual limb pain reported only 18% enrolment of eligible participants (Robinson *et al.,* 2004). This study may not have met its target recruitment rate because it was set unrealistically high. A participant rate of 42% is good and suggests a future definitive trial would be possible.

As identified in section 5.6.2, amputees have often undergone extensive unpleasant interventions prior to amputation, and this may partly explain the reason for those refusing to consent to receive an unnecessary additional intervention which was often perceived sceptically. Other studies have also identified that potential participants may not consent due to the additional demands of a trial, which may cause inconvenience and that participants may have concerns about the intervention and not wish to take part in an 'experiment' (Ross *et al.*, 1999). The ARU may not have been an optimal site for recruiting participants with it being a busy unit providing care for those at a key life point, who had recently undergone amputation. Although, overall, recruitment into the study was good, future studies may benefit by including amputees who are not in an inpatient unit receiving multiple other interventions and by making the proposed intervention less intensive. However, although inclusion of outpatients may aid recruitment, it may cause problems to arise which were not identified in this trial, such as problems with participation rates due to lack of assistance or strength to travel to the outpatient appointment (Ekman *et al.*, 1998).

6.7.3 Randomisation and blinding

Randomisation was successful in this study, but blinding was not. Blinding is necessary to avoid the introduction of performance and ascertainment bias and prevent reporting misleading results (Karanicolas *et al.*, 2010). Inadequate treatment allocation concealment has been found to yield larger estimates of treatment effect (Schulz *et al.*, 1995) and ideally, participants, clinicians, data collectors and data analysts should all be blinded. Blinding of data collectors ensures unbiased ascertainment of outcomes

(Karanicolas *et al.*, 2010) but was unsuccessfully implemented in this trial. Although this did not affect the results of this trial (as this trial was not evaluating the effectiveness of the intervention) this would need to be addressed before implementing a future definitive trial. A future trial would not be able to blind participants as sham interventions were not considered physiologically inert (section 6.4.2) and blinding of clinicians would not be possible. However, binding of data collectors and analysts could be addressed. In this study the data collector had close contact with clinical staff at the rehabilitation unit. A future study may benefit from the data collector having less close contact with clinical staff and clearly including information on the participant information sheet about the necessity of blinding. Alternatively, if blinding of data collectors was deemed impossible, a future trial should ensure that the outcome measures used are reliable and as objective as possible. Additionally, a future trial could use duplicate assessments of outcomes and report the level of agreement between assessors (Karanicolas *et al.*, 2010). If a future study was adequately funded, data analysts could be different personnel to data collectors, so ensuring blinding during analysis of results.

6.7.4 Acceptability of the intervention

Establishing acceptability and compliance is vital before commencement of a fully powered trial, as if the intervention is not acceptable and participants are not compliant, the study will fail. Some participants were initially sceptical about the study and despite volunteering to participate hoped they would not receive acupuncture intervention. This was unexpected as the qualitative descriptive study described in section 5.6.1 identified that amputees generally did not have concerns about acupuncture treatment and considered it a credible intervention. Also, data from an English nationwide survey found that lifetime prevalence of using complementary and alternative medicine was 44%, with massage, aromatherapy and acupuncture most commonly used (Hunt *et al.*, 2010). This data suggests that interventions such as acupuncture are acceptable and used by a substantial number of people in England. However, CAM tends to be used most by middle aged females with higher levels of education who have more than one health condition, but may not be more likely than non-users to have a specific condition (Bishop and Lewith, 2010). In the UK men are twice as likely as women to undergo

amputation and half of all amputations are performed on people aged 70 years or older (NHS, 2012). An American survey of self-reported treatments used for PLSd found only 15% used alternative modalities (massage, chiropractic care, hypnosis, acupuncture and naturopathic care) and of these only 1% had used acupuncture (Hanley *et al.*, 2006). This may explain participants' initial scepticism and negative views towards acupuncture intervention. In a definitive trial, as stated above, a brief introduction by clinical staff about acupuncture may make participants less sceptical of the intervention and more willing to consent.

Having a usual care control was in keeping with the MRC framework used in this project (Craig *et al.*, 2008a) and is considered suitable for pragmatic effectiveness trials of protocolised care (Thompson and Schoenfeld, 2007). Participants considered a usual care control acceptable, and only one participant dropped out of the study due to being randomised to usual care. Future studies should use a usual care control as it is acceptable, appropriate for pragmatic trials, has the advantage of being safe as physicians make individualised treatment decisions about participant care and unlike efficacy trials, ensures the intervention can claim to be superior to usual practice (Thompson and Schoenfeld, 2007).

Acupuncture was considered unpleasant in terms of the physical process of needle insertion but considered pleasant in terms of the feeling of relaxation obtained once the needles were inserted. Similar findings have been reported in other studies (Hopton *et al.*, 2014, Hopton *et al.*, 2013) with participants reporting needling discomfort but then feeling relaxed whilst the needles were in situ, suggesting the intervention should be acceptable in a definitive trial. Despite the qualitative descriptive study (section 5.6.1) identifying concerns about electro-acupuncture, in this study it was found to be acceptable and was generally perceived as beneficial, suggesting it should be included in a protocol for a definitive trial. Also, other studies suggest it may be effective for pain relief. A systematic review evaluating the effectiveness of acupuncture for post-operative pain identified 15 RCTs, of which six used electro-acupuncture, and reported positive findings (Sun *et al.*, 2008).

Acupuncture was perceived to be effective for treating PLSd, and generally was perceived to resolve symptoms within the eight allocated treatments. This is in keeping

with results from case studies (Hu *et al.*, 2014a, Mannix *et al.*, 2013) and non-randomised controlled trials (Hu *et al.*, 2014b). Although this study was underpowered to report on the effectiveness of the intervention, findings suggest acupuncture may reduce PLSd intensity, confirming the need for a definitive trial to determine the effectiveness of this intervention.

6.7.4.1 Adverse effects

An advantage of completing the feasibility study at the ARU was that it was in a safe environment and had participants had any adverse events, they were in an environment where this could be addressed immediately. Adverse effects, captured during semi-structured interviews were found to be minimal. Acupuncture was not considered to cause any serious adverse effects, and those effects which were reported (bleeding, bruising, needle insertion pain, flare up of symptoms) were those which are known and have been reported in other studies assessing acupuncture safety (Witt *et al.*, 2009, MacPherson *et al.*, 2004). These results suggest it would be safe to complete a definitive trial on amputees who are less closely monitored, including outpatient amputees.

6.7.5 Retention and compliance / adherence

Overall, participant retention and compliance with the acupuncture protocol was good up to the primary endpoint of the study. However, as described in section 6.6.5, due to poor practitioner compliance, no participants received all eight acupuncture treatments and treatment was often provided weekly instead of twice weekly. Many UK acupuncture case studies have reported positive outcomes providing treatment for PLSd once weekly for less than eight weeks (Bradbrook, 2004, Davies, 2013) and this may be a more appropriate dosage. Additionally this number and frequency of treatments was often perceived effective (section 6.6.4), suggesting fewer than 8 treatments, delivered weekly may be adequate, allowing the intervention to be more cost effective. However, further research is needed to generate empirical evidence on what would constitute an adequate dose. A clinical study comparing the effects of different treatment protocols may be the most reliable source of evidence and may demonstrate a dose-response relationship (White *et al.*, 2008). To establish the most effective physical treatment procedure, future dosage studies should follow the Standards for reporting

interventions in clinical trials of acupuncture (STRICTA) reporting recommendations (MacPherson *et al.*, 2010).

In keeping with the study protocol and the philosophy of TCM acupuncture, participants were treated holistically during the study and complaints other than PLSd were addressed over the course of treatment. It has been suggested that TCM acupuncturists do not always implement a holistic approach in clinical trials (Paterson and Britten, 2008) but this was not the case in this study. However, unexpectedly the acupuncture practitioner was found to not adhere to other aspects of the acupuncture protocol. No participants received all eight acupuncture treatments, auricular acupuncture was seldom used, acupuncture was usually administered to both the residual and contralateral limb, a segmental approach to treating dermatomal pain was seldom taken and participants were often only treated once weekly. This lack of practitioner adherence was not anticipated as during discussion with practitioners about the development of the trial protocol, practitioners were positive about the acupuncture protocol and willing to use it. This lack of adherence may have been partly due to tensions between clinical and research workload (Adams *et al.*, 2015) and due to poor researcher communication with the acupuncture practitioner team. This would need addressing before undertaking a definitive trial as lack of participants receiving the full intervention as intended could lead to reduced effectiveness, a decrease in study power and inappropriate conclusions (Chan *et al.*, 2013). Many trials include strategies to monitor and improve adherence and this approach would need to be taken with practitioners in a future trial. Robiner (2005) provides a table of adherence enhancing strategies, and although these are aimed at participant adherence, some could be used to help ensure practitioner adherence in a future trial, such as promoting collaboration and good communication between acupuncturists and research staff, providing feedback on adherence, promoting non-judgemental discussion around adherence (including barriers and facilitators) and addressing adherence problems proactively.

6.7.6 Outcome assessment

Although participants adhered to completing outcome measures whilst at the ARU and retention of participants during this phase of the study was good, this was not sustained post discharge and < 40% of participants completed the one month follow up

questionnaire. This lack of long term retention would need to be addressed before undertaking a definitive trial as poor retention has implications on statistical power and the internal and external validity of the study (Bower *et al.*, 2014). A systematic review identifying strategies to increase response to questionnaires identified that monetary incentives, recorded delivery, a teaser on the envelope (such as a comment on the envelope suggesting that it would benefit the participant), having an interesting questionnaire topic, pre-notification reminders, follow up contact, unconditional incentives, shorter questionnaires, providing a second copy of the questionnaire, mentioning an obligation to respond, university sponsorship, personalised questionnaires, hand-written addresses, assurance of confidentiality and first class outward mailing improved postal questionnaire response rate (Edwards *et al.*, 2009). In randomised controlled trials offering and giving small monetary incentives has been found to be successful in improving questionnaire response (Bower *et al.*, 2014). If ethical, a future study may need to provide incentives and may also improve response rates by including a follow up contact with participants, by including in the questionnaire a reminder of an obligation to respond and by resending the questionnaire to participants if necessary.

Although this study identified problems with participant retention at one month follow up, a definitive trial would need to include a longer term follow up to determine the long term effectiveness of the intervention. Although the strategies described above could be put in place to encourage retention, other factors need to be taken into consideration which may influence participant long term response. Lower limb amputees tend to be a frail population and in this study two participants were withdrawn due to being medically unwell. It is recognised that long term survival post lower limb amputation, regardless of the presence of diabetes mellitus is poor (Subramaniam *et al.*, 2005) and it has been estimated that by one year post amputation almost half (44%) of lower limb amputees will have died and by five years 77% (Fortington *et al.*, 2013). Additionally, major amputations are associated with high morbidity and complication rates (Ploeg *et al.*, 2005) possibly further affecting long term retention rates of a future RCT. This would need to be taken into consideration when designing a definitive trial.

This feasibility study identified that practitioner compliance of capture of adverse effects

was poor. Although adverse events were captured by the researcher, the acupuncture practitioner did not record adverse events in participant records. In RCTs reporting of adverse events is frequently found to be incomplete (Smith *et al.*, 2013) and this would need addressing before undertaking a definitive trial. Recommendations of capture of adverse events have been made by Ioannidis *et al.* (2004). These recommendations include capturing the frequency, incidence, timing and severity of each event. A future study may benefit from giving practitioners a log book designed to capture this information. Capture of rescue medication was not possible in this study as participants were not self-medicating and were often unsure what medication they were taking. Other studies also report that participants in an inpatient setting are not always in control or aware of the medication they are taking. A study involving three London hospitals found only 20% of patients had kept and administered their own medication whilst in hospital (Mohsin-Shaikh *et al.*, 2014). A future study would benefit from the researcher having access to inpatient participants' medical notes. Data would need to be captured on rescue medication as it can reduce the observed treatment effect in intention to treat analysis (White *et al.*, 2001).

6.7.7 Selection of most appropriate outcomes

The feasibility study identified appropriate outcome measures which could be used in a future definitive trial. The NRS (worst and average pain), SF-MPQ-2 and PGIC were all considered appropriate and manageable and were fully completed by all participants. The HADS, PSS-10 and EQ-5D-5L were not considered appropriate for the reasons stated above (section 6.6.7). However, although the HADS may have found participants' median depression and anxiety scores were normal because amputation can be viewed positively (Couture *et al.*, 2011 and section 5.6.2) this may not be the case. Scores may have been normal due to the way this outcome measure was collected. This outcome measure may be appropriate in a future trial, if data are collected without the researcher being present. It may also be appropriate on a different demographic group of amputees.

The ISI may be appropriate in a definitive trial as PLSd was identified in the previous qualitative descriptive study as causing sleep disturbances and acupuncture / acupressure may be effective at treating sleep disorders (Sarris and Byrne, 2011). As

acupuncture may improve sleep, future studies capturing participant medication and including outpatient amputees could still include a secondary outcome measure on sleep.

As both this study and the qualitative descriptive study (section 5.6.7) identified that the SF-MPQ-2 included some terminology which was not understood, an alternative outcome measure may be more appropriate in a definitive trial. Alternative outcomes measuring neuropathic pain quality which have been designed for use in clinical trials include the neuropathic pain scale (NPS), the neuropathic pain symptom inventory (NPSI), and the Pain Quality Assessment Scale (PQAS). NeuPSIG recommends using the NPS and NPSI as outcome measures in pain trials (Haanpää *et al.*, 2011) as does the European Federation of Neurological Societies (Cruccu *et al.*, 2010). The NPS was developed to describe neuropathic pain qualities and document the impact of pain treatment on pain in clinical trials. It includes 10 items, two of which assess global pain intensity and unpleasantness and eight that reflect pain qualities and characteristics (Jensen and Karoly, 2011). However, it does not include a number of pain qualities commonly associated with neuropathic pain such as shooting, tingling and electric pain (Jensen, 2006). The NPSI includes 12 items which assess four global domains of neuropathic pain and number of hours of spontaneous pain in the last 24 hours (Jensen and Karoly, 2011). Both these scales have been found sensitive to change in double blind trials (Haanpää *et al.*, 2011). The PQAS is a revised, expanded version of the NPS. It includes the NPS and a further 10 descriptors of pain, and measures both neuropathic and non-neuropathic pain. It has been shown to be valid in carpal tunnel syndrome for assessing treatment related changes in pain qualities (Jensen *et al.*, 2006). However, it is much longer than the NPS which may make it less acceptable.

6.7.8 Sample size calculation

The study did generate data allowing for a sample size calculation. As the study was conducted on a select group of participants (participants who were recent lower limb amputees) this data may not be appropriate for future studies on a wider demographic group. However, as past UK randomised controlled trials do not provide information on sample size calculation (Liaw *et al.*, 1994) this data is unique and should provide guidance for future studies.

To meet the sample size required for a definitive trial, a future study would need to be conducted at a larger unit than the ARU involved in this study, or take a multi-centred approach. If taking a multi-centred approach, assuming a future study allowed one year for recruitment and included rehabilitation units which were similar in size to the ARU and achieved a recruitment rate of 15 participants a year, a total of 12 units would need to be involved in a definitive trial. If outpatient amputees, and bigger units were included in a definitive trial, fewer numbers would need to be involved.

6.7.9 All components of the protocol work together

This study identified areas which would need addressing before undertaking a definitive trial. Difficulties were identified with recruitment, practitioner adherence to the protocol, completion of outcome measures at one month follow up and blinding. Considerations relating to these areas have been discussed above.

The study was possible due to its unique setting with an acupuncture department co-located in the same building as an ARU. If a definitive study was undertaken, it may be necessary to provide physiotherapists with training on the acupuncture protocol. Additionally, this study identified that environmental factors, such as where the acupuncture was conducted, rapport with the practitioner and the participants' state of mind were all considered to affect treatment, as was prosthesis use and acceptance of body image. Past research has also identified that treatment characteristics can affect outcome (Fraenkel, 2010) and rapport and positive participant involvement have been identified in other acupuncture studies as factors which affect outcome (MacPherson *et al.*, 2006). Supportive practitioners are more effective than neutral / formal practitioners (Fraenkel, 2010) and providing positive information significantly improves health outcomes (Di Blasi *et al.*, 2001). Past studies have also identified that prosthetic use can ease PLSd. A study comparing cosmetic to functional prosthesis use found functional prosthesis wearers exhibited a significant decrease in pain compared to the cosmetic group, possibly due to related cortical reorganisation in the functional prosthesis group (Weiss *et al.*, 1999). A future study would need to consider the environment where the intervention was to take place. A busy physiotherapy unit may not provide an optimal environment. Ideally, multiple practitioners should be used in a future study. Supplementary data on prosthetic use should be captured.

6.7.10 Further considerations when designing a definitive trial

As stated in section 6.4, as RCTs are considered to provide the most reliable type of evidence, this study aimed to inform the design of a future definitive RCT. However, there are many different types of study design, with different designs suiting different questions and circumstances. As acupuncture was considered a complex intervention, a RCT may not be the most appropriate type of study design to use in a future definitive trial. Alternatively, other designs, which are appropriate for use when evaluating complex interventions, such as preference trials, stepped wedge designs and cluster randomised controlled trials could be considered (Craig *et al.,* 2008a).

Preference trials are appropriate when patients have very strong views about a treatment. As participants in this feasibility study were willing to be randomised and as the MRC framework for developing and evaluating complex interventions advises randomising whenever possible (as this is the most robust method of preventing selection bias (Craig *et al.,* 2008a)) this would not be an appropriate design for a definitive trial. A stepped wedge design could be used in a future trial. It is appropriate when there is already some evidence of effectiveness and allows the intervention to be rolled out to a whole population. It is a pragmatic study design which is appropriate for evaluation of service delivery type interventions (Hemming *et al.,* 2015). However, as evidence supporting the effectiveness of acupuncture for treating PLSd is still sparse and as NHS stakeholders are not trying to roll out acupuncture treatment to all amputees with PLSd, this design may not be necessary. A cluster randomised trial may be the most appropriate design for a definitive trial. Using this design, in a future multi-centred trial, each rehabilitation site could be considered a unit of randomisation. This should ensure increased administrative efficiency, lessened risk of experimental contamination and increased likelihood of subject compliance (Donner and Klar, 2004). These features should outweigh the resulting loss in statistical precision associated with cluster randomised trials (Donner and Klar, 2004).

Summary of discussion

- To ensure full engagement and to ensure potential participants are not missed, clinical staff may need to allocate regular time to a future project.
- Communication skills of research staff can affect recruitment rates. Future trials need to ensure those recruiting have adequate skills in this area. Additionally, participant education about acupuncture may be necessary prior to recruitment.
- To ensure adequate numbers of participants are recruited a future trial may need to be multi-centred and include outpatient amputees. Also, the inclusion criterion PLSd ≥ 5/10 intensity may need reducing.
- Overall, the participation rate for this study was good, suggesting a future definitive trial would be possible.
- Blinding would need addressing in a future trial. Outcome measures should be reliable and valid and duplicate assessments of outcomes could be implemented.
- The acupuncture protocol used in this trial was acceptable and perceived to be effective, suggesting a fully powered trial would be possible. A usual care control is acceptable and should be used in future trials.
- Adverse effects from acupuncture were minimal, suggesting it would be safe to include both inpatient and outpatient amputees in a future trial.
- Less than eight treatments delivered weekly may be a more appropriate acupuncture dosage to use in a future trial, but this would need to be established through a dosage trial.
- Future trials need to implement strategies to ensure long term retention of participants and to ensure practitioners adhere to the study protocol and collect data on adverse events.
- The HADS, PSS-10, EQ-5D-5L may not be appropriate outcome measures to use in a definitive trial. The ISI may not be appropriate in an inpatient setting. The NPSI, NPS or PQAS could be used instead of the SF-MPQ-2. The PGIC should capture positive and negative change.

6.8 Limitations and methodological considerations

This study did not consider the effect of 'attention' on symptoms and did not include a control that mimicked the theoretically inactive elements of acupuncture, but not the active elements (Popp and Schneider, 2015). This was not done as the study was conducted under the MRC framework for complex interventions which recommends usual treatment rather than some form of placebo (Craig *et al.*, 2008a). However, qualitative findings suggested acupuncture may partly have been effective due to participants' relationship with the practitioner and the environment surrounding treatment (section 6.6.9). Other studies have reported similar findings, identifying the complexity of acupuncture (White *et al.*, 2008) the importance of a therapeutic alliance between patient and practitioner (Hopton *et al.*, 2013) and the development of rapport (MacPherson *et al.*, 2006). Further research would need to be carried out to identify which aspects of acupuncture intervention cause change and whether environmental factors effect outcome (such as treatment setting and whether one to one treatment produces different therapeutic effects to group treatment). A future RCT may benefit from taking a three armed approach as in a study by Huang *et al.* (2011) including a usual care group, an acupuncture group and an attention group.

The study did not recruit the number of participants it initially aimed to recruit. However, this was not viewed as a limitation as it still managed to meet its objectives. Also, as it was a feasibility study it never aimed to provide data on effectiveness. It is recognised that quantitative findings reported in this study should be interpreted with caution.

Although two acupuncture practitioners were meant to be involved in the feasibility study, in reality only one was. As differences in effectiveness have been observed between different practitioners (Wampold and Serlin, 2000) and found to be greater in treatments involving greater psychosocial emphasis (Lewis *et al.*, 2010) future studies would benefit from use of multiple practitioners.

Acupuncture was meant to be delivered twice weekly at the end of the day (4.30pm) to avoid disrupting participants' usual care. However, practitioners did not adhere to this and acupuncture was provided throughout the day. This meant appointments could not

be scheduled into participants' diaries and treatment was provided on an ad hoc basis meaning participants were not offered 8 treatments.

Two participants in the acupuncture group were not interviewed. Although qualitative samples are usually small, as only five participants were interviewed, data saturation could not be assumed. It was unclear if new evidence would have emerged from further interviews.

The feasibility study protocol did not include interviewing the usual care group or acupuncture practitioners involved in the trial. Interviewing the usual care group would have provided useful data on their experience of being involved in the trial. Interviewing practitioners may have helped identify issues around lack of compliance with the acupuncture protocol. A future definitive trial, if using MMR, may benefit from collecting data from both the usual care group and acupuncture practitioners.

6.8.1 Quantitative methodological considerations

In quantitative studies bias should be accounted for as it can affect the reliability and validity of the data (Parahoo, 2014). The Cochrane Collaboration tool for assessing risk of bias was used to determine the risk of bias in this study (Higgins and Altman, 2008). Selection bias was considered low in that the study achieved generation of a random number sequence and allocation concealment prior to group assignment. However, selection bias could be considered high in that the study population were all from an inpatient rehabilitation unit and this may not be representative of the wider population of interest (Bowling, 2002). The study had a high risk of performance bias as blinding of participants and acupuncture practitioners was not possible. Also, blinding of the researcher collecting outcome measures was not successful. The study also had high risk of detection bias as the outcome assessor was not blinded to the knowledge of which intervention participants received. In a larger study, if adequate funding was available, independent outcome assessors would be included in the study protocol. Attrition bias was considered low at the primary end point of the study as only one participant dropped out of the study and two were withdrawn and all participants who were enrolled and not withdrawn / dropped out completed all outcome measures weekly for the duration of the study. However, attrition bias at one month follow up

was high with only 5 participants completing and returning postal outcome measures. Also, as stated in section 6.5.9, LOCF may not have been the most robust method of dealing with missing data and other methods may be considered more appropriate in a larger definitive trial. The researcher tried to avoid reporting bias and selective reporting of outcomes, and all pre-specified outcomes were reported on. In keeping with quantitative research, the view that the investigator and investigated are separate entities was taken and the researcher did not recognise her positive bias towards acupuncture as affecting the study outcomes.

6.8.2 Qualitative methodological considerations

Credibility of findings were reduced as data saturation could not be ensured. The researcher was explicit about the underlying philosophy and methodology of the study and was aware that her biases, goals and *a priori* knowledge may have distorted findings (Savin-Baden and Howell Major, 2013). No formal member checking was undertaken for the reasons reported in section 5.5.4.1 and this potentially reduced the credibility of findings. Peer debriefing took place throughout the research process, ensuring the researcher's biases were probed and interpretations clarified (Shenton, 2004). Triangulation of qualitative and quantitative findings using side-by-side comparison enhanced credibility of findings (Tracy, 2010) as did the use of framework analysis, ensuring capture of negative cases. Transferability of results may have been reduced due to the small number of participants interviewed. However, those interviewed were of mixed gender, age and ethnicity allowing for a range of information to be collected (Ritchie *et al.*, 2003). Findings could be considered dependable as the processes involved in the study were reported in detail, clearly documented and were auditable (Shenton, 2004). Confirmability was assumed as the researcher strived to report the experience of participants and not the preferences of the researcher (Shenton, 2004).

Summary of study limitations and methodological considerations

- The study did not identify which aspects of acupuncture intervention causes change and whether environmental factors affect outcome.
- Only one acupuncture practitioner treated participants during the trial.
- The acupuncture protocol was not adhered to.
- Quantitatively the trial had a high risk of bias in multiple areas.
- Qualitatively data saturation could not be ensured.

6.9 Conclusion

The study was original and provided novel data on the feasibility of conducting a RCT to establish the effectiveness of acupuncture intervention for treating lower limb amputees with PLSd. The study achieved its objectives, establishing that the protocol used in this study was acceptable, informed that a sample size of 85 per group would be necessary for a future definitive trial and outcome measures were identified which could be used in a definitive trial. Additionally, preliminary data from this study suggests the acupuncture protocol is safe and would be suitable for use in routine care.

Before undertaking a definitive trial, recruitment, practitioner adherence to the acupuncture protocol, completion of outcome measures at one month follow up and blinding should be addressed. Recruiting participants was identified as problematic due to the inclusion criterion requiring participants to have PLSd ≥ 5/10 intensity, potential participants being sceptical about acupuncture and being unwilling to be involved in a RCT and busy clinical staff not identifying all potential participants. Future studies would need to address these areas. Using a cluster randomised trial design may help address some of these problems. Acupuncture practitioners were poor at adhering to the study protocol, especially in relation to frequency and total number of treatments provided. Future studies would need to ensure greater communication between researchers and practitioners to ensure identification and resolution of problems preventing practitioner adherence. To ensure completion of outcome measures post completion of the intervention strategies may need to be put in place, such as pre-notification reminders and follow up contact with participants. Frailty of this demographic group may affect long term follow up in a definitive trial. As blinding may be problematic, future trials could use duplicate assessments of outcomes and report the level of agreement between assessors. Additionally, further study is needed to identify which component parts of an acupuncture treatment are effective and to establish optimal acupuncture dosage.

Summary of feasibility study

- The acupuncture protocol used in this study was acceptable and perceived to be effective.
- To ensure adequate recruitment of participants, a future trial may need to be multi-centred, include both inpatient and outpatient amputees, lower the inclusion criterion of PLSd ≥ 5/10 and ensure trial centres allocate regular time to the trial.
- The NRS, PGIC and SF-MPQ-2 (or NPSI, NPS, PQAS) are appropriate outcome measures which could be used in a definitive trial. A measure of sleep could also be included.
- Greater communication is needed between acupuncture practitioners and researchers to ensure protocol adherence.
- Strategies need to be put in place, such as pre-notification reminders and follow up contact with participants to ensure long term retention of participants.
- As blinding may be problematic, future trials should consider including duplicate assessments of outcomes and report the level of agreement between assessors.
- Further research is needed to establish optimal acupuncture dosage for treating PLSd.

Chapter 7. Conclusion

7.1 Introduction

The previous three chapters described three separate studies undertaken sequentially using a MMR multiphase design to inform the development and feasibility of a definitive RCT. The first two studies were a Delphi consensus study, undertaken to develop a treatment protocol, and a qualitative descriptive study, exploring the perceived acceptability of acupuncture and willingness to be involved in RCT within the context of living with PLSd. Both these informed the development of the third, a study which evaluated the feasibility and acceptability of undertaking a definitive trial. These separate studies were undertaken in keeping with the developmental and feasibility / piloting stages of the MRC framework for developing and evaluating complex interventions (Craig *et al.*, 2008a) prior to undertaking a definitive trial.

This chapter summarises this project's original contribution to new knowledge. It refers back to the project objectives (listed in figure 1.2) and draws meta-inferences on recommendations for a future definitive trial which could be used to assess the effectiveness of acupuncture intervention for PLSd. It identifies weaknesses and strengths of the MMR multiphase design using Onwuegbuzie and Johnson (2006) legitimation criteria and suggests areas for future research in keeping with the MRC framework for developing and evaluating complex interventions.

7.2 Original contribution to new knowledge

The project produced original data in each of the studies undertaken within its theoretical and methodological framework. The project developed a novel acupuncture protocol for the treatment of lower limb amputees with PLSd. New knowledge on amputees' experience of PLSd was developed. An original RCT evaluated the feasibility and acceptability of acupuncture intervention for treating amputees with PLSd, providing novel data in preparation for a definitive multi-centred randomised controlled trial.

The literature review reported in chapter 2 ascertained that current evidence on the management and prevention of PLSd is limited, identifying the need for further research to determine effective methods. Currently evidence does not support the use of pre-emptive interventions and studies are limited on the effectiveness of pharmacological interventions to manage PLSd. Deep brain stimulation does not appear to be beneficial for chronic pain and evidence on the effectiveness of GMI and mirror therapy although positive is limited. Evidence on the effectiveness of acupuncture specifically for managing PLSd is also sparse. Only two non-randomised controlled trials were identified, both of which were deemed to have high risk of bias and low methodological quality. These findings highlighted the need for future research evaluating the effectiveness of interventions such as acupuncture for treating PLSd. This project developed novel developmental data, required before undertaking a definitive trial evaluating the effectiveness of acupuncture for treating this syndrome.

During the literature search, reported in section 2.7, the case studies identified provided little guidance on what constituted good acupuncture practice when treating PLSd. This ascertained that further research was needed to gain consensus on treatment guidelines which could be considered 'good practice'. The first study described in this project (Chapter 4) developed a novel and original protocol, which could be used both in research and in clinical practice. It provided guidelines on 'good practice' which were not previously available. The study established new knowledge on acupuncture treatment, gaining consensus that qi and blood stagnation were underlying pathologies of PLSd. It identified that treatment principles should include moving qi and blood as well as managing and reducing pain and treating the individual's specific pathologies.

There was consensus on the use of a combination of body and auricular acupuncture, needling the contralateral limb and on the use of some specific points. Consensus was met on a needle retention time of 20-30 minutes and a treatment frequency of weekly or twice weekly for at least six treatments.

The literature review described in section 2.5 identified that few studies have been conducted exploring amputees' experience of PLSd. It established that those that have tend to be of low reporting quality, not specific to lower limb amputees, and not specific to a UK population. Also, during this literature search no studies were identified exploring the acceptability of acupuncture for treating PLSd. This ascertained the need for further methodologically sound research to explore amputees' experience of PLSd and the perceived acceptability of acupuncture within a specific demographic group of amputees. The second study (described in chapter 5) provided new knowledge on a UK demographic group of amputees' experience of PLSd shortly post amputation. It provided an original and rich account of this syndrome, identifying PLSd to be 'real' with kinetic, kinaesthetic and exteroceptive perceptions which were burdensome to participants. PLSd was often described as a feeling of the limb being bound in a vice or tightly squeezed. Although PLSd was usually perceived negatively, it could also be perceived positively, providing new knowledge which may be useful to clinicians treating this condition. PLSd was found to affect sleep, mood and wellbeing and was often not relieved through medication. Up to date data were generated on the adequacy of information provided to amputees, providing useful information on the need for this to be better addressed in clinical practice. Additionally, data were generated on the experience of amputation and suffering pre-amputation. The study presented novel data on the acceptability of acupuncture for treating PLSd, finding acupuncture to be generally considered a potentially acceptable intervention. Additionally, outcome measures were identified which could be used in a RCT. Overall, the study provided an original and detailed account of the acceptability of acupuncture for treating PLSd and on the experience of PLSd in recent lower limb amputees, establishing that acupuncture was perceived as an acceptable intervention and that PLSd was bothersome and poorly managed.

The study reported in chapter 6 was original, providing novel data on the feasibility of

conducting a RCT to determine the effectiveness of acupuncture for treating PLSd. No previous RCTs or feasibility/ pilot studies were identified, meaning findings from this study provided new knowledge. These data should be useful to researchers looking to undertake a definitive trial evaluating the effectiveness of acupuncture for treating PLSd. The study produced original data identifying that in a definitive trial strategies would need to be put in place to enhance recruitment of participants. Randomisation should be acceptable as should having a usual care control. Acupuncture should be an acceptable intervention and participant retention should not be problematic. However, findings from the feasibility study suggest that treatment may be more acceptable and equally as effective if administered once weekly for approximately 6 weeks. The feasibility study identified outcome measures which could be used in a definitive trial and data were generated, allowing for a sample size calculation to be undertaken. The study identified that strategies, possibly including incentives, would need to be put in place in a definitive trial to ensure long term follow up of participants was achieved. Strategies would also need to be put in place to ensure practitioner adherence to the study protocol. Table 7.1 summarises meta-inferences drawn from the feasibility study, providing original guidance for the design and development of a fully powered RCT.

Summary of original contribution to new knowledge

- An acupuncture protocol was developed for the treatment of PLSd, providing novel guidelines on 'good practice' which did not previously exist.
- An original and detailed account on the perceived acceptability of acupuncture was reported as was the experience of amputation / PLSd in a UK lower limb specific population.
- A study was undertaken to evaluate the feasibility and acceptability of acupuncture for treating PLSd. This was original and provided novel data on the feasibility and acceptability of this intervention, providing original guidelines for a definitive trial.

Table 7.1 Guidelines for the design and development of a fully powered RCT evaluating the effectiveness of acupuncture for treating phantom limb syndrome

Methodological issues	Implementation strategies
Trial design	A pragmatic effectiveness study of parallel design with usual care control is acceptable. A three armed trial including usual care, acupuncture and attention could provide information on the component parts of acupuncture. A three armed trial providing different dosages of acupuncture could inform on optimal dosage.
Participants	Widen the inclusion criteria to allow for recruitment of a larger sample size; possibly offer treatment irrespective of pain intensity, recruit and include out-patient amputees and amputees with chronic PLSd.
Recruitment	Ensure clinical staff at study sites allocate regular research time to ensure identification of all potential participants. Provide some form of information to amputees about acupuncture prior to enrolment in the study. Include participants who are not inpatients and receiving multiple other interventions at the time of the study. Ensure research staff have adequate knowledge about the study and communication skills when recruiting participants. Include multiple sites to ensure adequate sample size is achieved.
Randomisation and allocation concealment	Use a computer generated random numbers table and sequentially numbered opaque sealed envelopes.
Sample size	Allowing for a 20% dropout rate, assuming a future study uses; a parallel RCT design, an 11 point NRS rating average intensity of PLSd over the last week to compare acupuncture versus usual care at four weeks, a two tailed independent sample T Test, a power and level of significance / α-level of 0.8 and 0.05 respectively, a sample size of 85 per group would be needed.

Methodological issues	Implementation strategies
Blinding	Ensure the necessity and importance of blinding is clearly explained to participants and clinical staff and is clearly documented on the PIS. If possible employ independent research staff to analyse data.
Acupuncture protocol	Use the protocol developed in the Delphi consensus study but include the use of electro-acupuncture and treat weekly for approximately six treatments. Ensure upcoming acupuncture appointments are clearly written down for participants and possibly provide reminders of upcoming appointments. Ensure acupuncture appointments are scheduled in advance and arranged at a mutually convenient time. Ensure acupuncture is provided in a quiet / relaxed environment.
Practitioner compliance	Ensure practitioners are educated on the use of the protocol. Promote collaboration between practitioners and research staff and hold group meetings. Provide feedback on adherence to the study protocol. Promote non-judgemental discussion around adherence including barriers and facilitators and address adherence problems proactively.
Participant compliance	If considered ethical provide incentives to encourage long term commitment to the study and completion of outcome measures post completion of the intervention. To encourage long term commitment include a researcher follow up contact with participants. Include in any postal questionnaires a reminder of an obligation to respond.

Methodological issues	Implementation strategies
	Be aware that lower limb amputees are a frail group with a high incidence of mortality and morbidity one year post amputation.
Outcome measures	Include the outcome measures; NRS and PGIC. Include ISI if participants are outpatients. Include either the SF-MPQ-2, NPS, NPSI or the PQAS. Ensure wording of PGIC is simple and include a scale which captures both positive and negative change.
Assessment of adverse events	Advise practitioners on the importance of capturing adverse events. Provide a log book for practitioners to capture the frequency, incidence, timing and severity of each event.
Assessment of use of rescue medication	If including inpatient participants in the study ensure the researcher has ethical approval to access participant medical notes / medication details.

Key: PLSd, phantom limb syndrome; PIS, participant information sheet; NRS, numerical rating scale; SF-MPQ-2, short form McGill pain questionnaire 2; PGIC, patient global impression of change; NPS, neuropathic pain scale; NPSI, neuropathic pain symptom inventory; PQAS, Pain Quality Assessment Scale.

7.3 Legitimation of the project

As reported in section 3.5, strengths and weaknesses of the project were evaluated using Onwuegbuzie and Johnson (2006) legitimation criteria.

There is debate as to whether qualitative and quantitative approaches can be combined due to the opposing paradigms they traditionally occupy (Onwuegbuzie and Johnson, 2006). Qualitative research usually takes a subjective epistemological stance, ontologically recognises there are multiple realities and axiologically views research as value bound. Conversely, quantitative research usually takes an objective epistemological stance, ontologically assumes there is one reality and axiologically believes research is value free (Onwuegbuzie and Johnson, 2006). In this study the researcher overcame this issue by taking a moderate philosophical position, namely pragmatism (section 3.3). In keeping with pragmatism, the researcher took the view that choosing a combination of qualitative and quantitative methods was appropriate and acceptable as this was the best way to answer the aim of the research (Greene, 2007). Through being explicit about the paradigm which this project was situated under, and through conducting all stages of the research within the assumptions of this paradigm, the researcher aimed to achieve paradigmatic legitimation.

The researcher took a view of commensurability, believing it is possible to switch between a qualitative and quantitative lens, allowing for findings and meta-inferences to go beyond either a purely qualitative or quantitative viewpoint. Taking a pragmatic stance allowed the researcher to develop meta-inferences and conclusions based on a moderate way of thinking which was not solely qualitative or quantitative. However given the researcher was a novice, this switching between qualitative and quantitative methods was difficult.

The project aimed to be explicit about the weight given to different components of each study, the mixing of data and the sequential approach taken and the researcher aimed to conduct the research rigorously / persuasively. However, there were sample integration weaknesses supporting the argument that inferences from the qualitative component of a study should not be transferred into generalisable findings during the integration of qualitative and quantitative findings (Onwuegbuzie and Johnson, 2006).

Generalising findings from the qualitative descriptive study to inform the acceptability of the feasibility study may not have been appropriate and may explain why findings on perceived acceptability of acupuncture and actual acceptability and participation in the feasibility study were different.

As the project included both qualitative and quantitative components, findings included both *emic* viewpoints (the viewpoint of the participant) and *etic* viewpoints (the viewpoint of the 'objective' outsider) (Onwuegbuzie and Johnson, 2006). Although inferences were not combined between studies, qualitative and quantitative data were combined in the feasibility study. Onwuegbuzie and Johnson (2006) recommend both the research team and participants review these meta-inferences to ensure insider-outsider legitimation. However, this was not done in this study and only the research team reviewed and discussed findings. A future study should include patient / public involvement.

As the project took a sequential multi-phase design weakness minimisation was not possible. Weaknesses of one study could not be compensated for by strengths of another to obtain a higher order meta-inference, as each study was evaluating different areas.

Apart from in the Delphi study, qualitative data were not transformed to quantitative or vice versa as this was not deemed appropriate for this project's design. However, if a future definitive RCT used MMR and included both quantitative outcome measures and qualitative data on perceived effectiveness of the intervention, data conversion may provide additional validity to meta-inferences.

A strength of the project was that the acupuncture protocol developed in the Delphi consensus study achieved validity on its acceptability and perceived effectiveness in the feasibility study. However, in reality as practitioners in the feasibility study did not adhere completely to the protocol, this affected its multiple validity legitimation. Another advantage of the project was that only one researcher was involved, so avoiding any tensions around ideology between qualitative and quantitative researchers and conflicts between researchers due to any paradoxes between qualitative and quantitative findings. However as stated above this was also seen as a limitation due to

the researcher having to switch between qualitative and quantitative methods throughout the research project.

7.4 Implications for future research and clinical practice

This project completed two stages of the MRC framework for developing and evaluating complex interventions, the developmental and feasibility / piloting stage. Further research would need to be undertaken to evaluate the effectiveness of acupuncture for treating PLSd, to assess cost-effectiveness and to understand change processes before implementation.

To evaluate effectiveness, a future RCT would need to be undertaken following the recommendations reported in table 7.1. As no research has currently been undertaken evaluating optimal dosage of acupuncture intervention for treating PLSd, it may be appropriate for a future trial to have several arms comprising of different acupuncture doses. Alternatively, a future parallel RCT could compare different acupuncture approaches such as only auricular acupuncture, body acupuncture alone or a combination of auricular and body acupuncture. Pharmacologically studies have taken both a preventative approach and management approach (section 2.6) and this approach could also be evaluated using acupuncture. Pre-emptive acupuncture could be trialled. The feasibility study identified that the acupuncture environment impacted on treatment (section 6.6.9). Future research could compare different acupuncture environments, such as group acupuncture versus one to one acupuncture. Other studies have identified that group acupuncture is acceptable (Simcock *et al.*, 2009) and it may provide additional benefits and should be more cost-effective than one to one treatment.

Although the project did not aim to directly change or improve clinical practice, findings could influence clinical practice. Despite acupuncture being a recommended treatment option for PLSd (Le Feuvre and Aldington, 2014) no clinical guidelines on acupuncture previously existed. This project developed an acupuncture protocol, agreed through consensus, for the treatment of lower limb amputees with PLSd. This protocol could be considered ‘good practice’ and could be used both in clinical practice and in a research setting. The protocol is novel, providing practitioners in clinical practice with guidelines which were not previously available. Additionally, the use of the protocol in the feasibility study established that it is safe, acceptable and perceived to be effective, providing practitioners with a tried and tested treatment option when treating PLSd. To

allow for implementation of acupuncture to be integrated into routine care NHS physiotherapists may require training on the Delphi protocol.

The project suggested that acupuncture may be perceived sceptically by some amputees with no past experience of it. In clinical practice this barrier to treatment may need addressing to ensure amputees can make informed decisions about their treatment options.

Qualitative studies exploring amputees' experience of PLSd are sparse, often of poor methodological quality and often not conducted within the UK (section 2.5). Although this project did not primarily aim to provide clinicians with insight into a UK demographic group of amputees' experience of amputation and PLSd, findings from the qualitative descriptive study did provide this information. These findings may help clinicians have greater understanding of PLSd. This stage of the project also identified that amputees' educational needs about PLSd are currently not being met, suggesting that changes need to be implemented in clinical practice.

7.5 Final summary

The project aimed to develop an acupuncture protocol for the treatment of lower limb amputees with PLSd and evaluate the feasibility and acceptability of this protocol in preparation for a definitive multi-centred randomised controlled trial.

The project was original, with only two previous underpowered non-randomised controlled trials identified evaluating the effectiveness of acupuncture for treating PLSd. This project was considered necessary as PLSd is a prevalent condition which is poorly managed pharmacologically. The project situated itself under the MRC framework for developing and evaluating complex interventions, using a multiphase MMR design.

The project achieved its objectives and developed, with acupuncture practitioners, an acupuncture protocol for the management of PLSd, which could be considered 'good practice'. Amputees' experience of PLSd was explored and found to be bothersome, affecting wellbeing. Acupuncture was perceived to be an acceptable intervention for PLSd and amputees were willing to be involved in RCT. Outcome measures were identified by amputees for use in a feasibility study. A feasibility study was completed informing that the acupuncture intervention was acceptable and perceived to be effective. Areas which would need addressing before undertaking a definitive trial were identified.

Summary of conclusion

- Research on the pharmacological and non-pharmacological management of PLSd is limited.
- PLSd is often viewed negatively by amputees and is considered a bothersome condition which affects wellbeing.
- Acupuncture is perceived to be an acceptable intervention for treating PLSd.
- Findings suggest that the acupuncture protocol developed in this project may be effective, is acceptable and could be used both in clinical practice and in future research.

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Appendix 2.1 Literature search strategy for qualitative papers exploring the experience of phantom limb syndrome

Pubmed

1. “Phantom Limb”[MeSh]
2. qualitative OR interviews OR “grounded theory” OR “thematic analysis” OR phenomenolog* OR “focus group*”
3. 1 AND 2

AMED

1. “phantom limb”.af OR “phantom pain”.af
2. qualitative.af OR interviews.af OR *"grounded theory".af OR "focus group*".af OR "thematic analysis".af OR phenomenolog*.af
3. 1 AND 2

CINAHL

1. (MH "Phantom Limb") OR (MH "Phantom Pain")
2. TX qualitative OR TX interviews OR TX "focus group*" OR TX "thematic analysis" OR TX "grounded theory" OR TX phenomenolog*
3. 1 AND 2

Medline

1. TX "phantom limb" OR TX"phantom pain"
2. TX qualitative OR TX interviews OR TX "focus group*" OR TX "thematic analysis" OR TX "grounded theory" OR TX phenomenolog*
3. 1 AND 2

PsycINFO

1. TX "phantom limb" OR TX"phantom pain"
2. TX qualitative OR TX interviews OR TX "grounded theory" OR TX "focus group*" OR TX "thematic analysis OR TX phenomenolog*
3. 1 AND 2

ScienceDirect

1. TITLE-ABSTR-KEY("phantom limb" OR "phantom pain") AND TITLE-ABSTR-KEY(interviews OR qualitative OR "grounded theory" OR "focus group*" OR "thematic analysis" OR phenomenolog*)

Appendix 2.2 Literature search strategy for systematic reviews on the management of phantom limb syndrome

Pubmed (1)

1. "Phantom Limb"[MeSh]
2. "chronic pain"[Title/Abstract]
3. 1 OR 2
4. "meta-analysis"[Title/Abstract]
5. "systematic review"[Title/Abstract]
6. 4 OR 5
7. 3 AND 6

Pubmed (2)

1. "Meta-Analysis" [Publication Type]
2. "Review" [Publication Type]
3. 1 OR 2
4. "Phantom Limb" [Mesh]
5. 3 AND 4

AMED

1. "phantom limb".ab.
2. "phantom pain".ab.
3. "chronic pain".ab
4. 1 OR 2 OR 3
5. "systematic review".ab.
6. "meta-analysis".ab
7. 5 OR 6
8. 4 AND 7

CINAHL

1. AB "phantom limb"
2. AB "phantom pain"
3. AB "chronic pain"
4. 1 OR 2 OR 3
5. AB "systematic review"
6. AB "meta-analysis"
7. 5 OR 6
8. 4 AND 7

Appendix 2.3 Characteristics of studies included in the review of systematic reviews

Citat-ion	Population (amputation specific)	Timing of intervention	Intervention	Control	Outcomes (relevant to measuring changes in pain or patient reported improvement)	Results	Adverse effects
Pre-emptive interventions							
Andrea and Andrea (2012)	1090 (211) participants undergoing elective surgery; shoulder, thoracotomy, breast cancer, plastic surgery of the breast, iliac crest bone graft, laparotomy, caesarean, hernia repair, prostatectomy, vasectomy, limb amputation.	Varied; Preoperative, post-incision, postoperative, preoperative continuous postoperative, post-incision continuous postoperative.	Varied type and dosage of drug administered by: epidural anaesthesia, paravertebral block, regional anaesthesia techniques, spinal anaesthesia, plexus block, nerve block and nerve sheath irrigation, vas deferens injection, topical application, local infiltration and wound or situs irrigation.	Conventional pain control, intravenous local anaesthetics (1 study).	Dichotomous outcome, continuous pain scales VRS, NRS, VAS, complex outcomes MPQ, SF-36. Outcomes collected at ≥ 5-6m follow-up.	Positive for epidural anaesthesia for open thoracotomy. Positive for paravertebral block for breast cancer surgery. Inconclusive for other surgical interventions or regional anaesthesia techniques.	Of the included studies reporting was sparse, sporadic and anecdotal, not prospective and systematic.
Chaparro et al. (2013)	4818 (175) participants undergoing surgery; breast surgery, hip or knee arthroplasty, abdominal or pelvic surgery, amputation, thoracotomy, heart surgery, spine surgery, thyroidectomy, inguinal herniorrhaphy, haemorrhoidectomy, a combination of different surgical procedures.	Varied; Preoperative, intra-operative, postoperative.	Drugs administered systemically by any dose, route or frequency: ketamine, (S)-ketamine, gabapentin, pregabalin, mexiletine, ibuprofen, amantadine, dextromethorphan, lidocaine, memantine, venlafaxine, nitrous oxide, opioids, corticosteroids: dexamethasone, methylprednisolone, hydrocortisone.	Placebo, compare several different active treatments (1 study)	Any surgical site pain three or more months after surgery using a 0 to 10 pain intensity scale, a categorical pain scale or report of movement evoked pain at ≥ 3m post surgery.	Positive for perioperative ketamine (if administered for > 24h), but results should be viewed with caution due to clinical heterogeneity of studies (surgical procedure, drug dose, treatment duration, trial populations). Negative for gabapentin, pregabalin and other studied drugs.	6/40 studies reported participants dropping out due to adverse events. Small numbers of dropouts were reported in pregabalin and gabapentin studies and larger numbers in ibuprofen studies.

Ypsilantis and Tang (2010)	442 (442) participants undergoing lower limb amputation due to peripheral vascular disease.	Varied; Preoperative, preoperative continuous postoperative, post-incision continuous postoperative, postoperative.	Local anaesthetics (Bupivacaine, Ropivacaine), opiates (Morphine, Diamorphine), NMDA receptor antagonists (ketamine), a2-agonists (clonidine) and GABA analogues (gabapentin) administered separately or in combination through the oral, IV, epidural or regional (perineural) route.	Various analgesics, opioids on demand, Bupivacaine.	*Prevalence of PLP and stump pain, intensity of PLP and stump pain (VAS, NRS), opioid analgesia requirements, reported complications, morphine requirements, multidimensional score (MPQ). Outcomes collected 1d – 1y post-surgery.	Inconclusive due to poor study design and small sample sizes. No evidence supporting the use of pre-emptive analgesia to minimise the risk of chronic pain post amputation.	The review did not report on adverse events of included studies.
Mixed interventions							
Humble, Dalton and Li (2015)	2834 (263) participants undergoing / undergone amputation, thoracotomy or mastectomy.	Not specified	Varied type of drug administered by any dose, route or frequency; mexiletine, gabapentin, gabapentin + ripivacaine + local anaesthesia cream, venlafaxine, ketamine, ketamine + bupivacaine, levobupivacaine + fentanyl + ketamine, epidural analgesia + cryonalgesia, PCA + cryoanalgesia, lidocaine infiltration, ropivacaine infiltration, lidocaine IV bolus + infusion, EMLA cream, epidural bupivacaine + morphine, paravertebral block, different regimes incorporating epidural or fentanyl PCA, mepivacaine, different epidural regimes.	Placebos (sham cream, sham block, saline), compared several different active treatments, conventional pain control.	*Pain intensity (VAS, NRS, VRS), pain at rest and movement, quantitative sensory testing, multidimensional score (MPQ). Time points for collection of outcome measures not specified.	Positive for gabapentinoids, antidepressants, local anaesthetics and regional anaesthesia for reducing acute and chronic pain. Negative for ketamine and cryoanalgesia for reducing chronic pain. Inconclusive for TIVA and opioids.	The review did not report on adverse events of included studies.

Halbert, Crotty and Cameron (2002)	375 (375) participants undergoing / undergone upper or lower limb amputation for various pathologies or trauma.	Varied: preoperative, preoperative-postoperative, intra-operative, <2w postoperative, >2w postoperative.	Varied; lumbar epidural, epidural infusion of bupivacaine + clonidine + diamorphine, epidural bupivacaine + morphine, regional analgesia + opioid analgesics, continuous postoperative regional analgesia, infusion of bupivacaine hydrochloride, IV infusion of ketamine, Salmon calcitonin infusion, TENS, farabloc stump liner, vibratory stimulation.	Conventional pain control, compare several different active treatments, placebo.	*Dichotomous variable for PLP, PLS, stump pain, intensity of PLP, stump pain (VAS), adverse events, mean opioid requirements, parenteral narcotic doses, morphine usage, multidimensional score (MPQ), subjective opinion, pain relief >50%, pressure pain thresholds, wind up pain, thermal stimulation, temporal summation of heat induced pain, reaction time. Time points for collection of outcome measures varied from post intervention - 1y.	Inconclusive due to study quality and contradictory results. Negative for pre-emptive epidurals.	Low prevalence reported: epidural, regional anaesthesia, High prevalence reported: salmon calcitonin, vibratory stimulation, IV ketamine at >2w postoperatively.
Pharmacological interventions							
Abbas (2012)	89 (89) amputees (reason for amputation not specified).	Varied; intervention when PLP ≥ 6m, amputation ≥ 6m, 1d post amputation.	Gabapentin for 30d, gabapentin for 6w titrated to a 2400-3600mg daily (study dependent) or maximum tolerated dose.	Placebo, placebo + conventional pain control.	*Intensity of PLP, stump pain using a pain rating scale (VAS, NRS), subjective assessment of pain increase / decrease, PLP frequency, number, duration. Outcomes collected post intervention and 7d-6m post treatment.	Positive, oral gabapentin may decrease PLP	Adverse events similarly reported in both the active and control arm.

Alviar, Hale and Dungca (2011)	255 (255) amputees due to traumatic, neoplastic, infections and chronic pain syndromes.	Varied; intervention when amputation ≤ 1w - 57y. PLP <1w - 49y.	Pharmacologic agents to treat (not prevent) PLP including; beta-blockers, calcitonins, analgesics, anticonvulsants, antidepressants, SSRIs, anaesthetics, NSAIDs, opioids, tramadol, topical analgesics, NMDA receptor antagonists, muscle relaxants, nerve blocks given singly or in combination in any dose, by any route.	Placebo, compare different active treatments.	Change in pain intensity from start of treatment to follow up points after treatment (VAS, NRS, number of persons with ≥ 30% or >50% pain relief, numbers needed to treat to benefit for 30%/50% pain relief, pain questionnaires). Time points for collection of outcome measures in double blind phase ranged 30min-6w. Other time points not specified.	Overall inconclusive for the short and long term effects of opioids, NMDA receptor antagonists, anticonvulsants, antidepressants, calcitonins and anaesthetics. Positive for morphine, ketamine and possibly gabapentin for short term analgesic efficacy. Negative for memantine and amitriptyline.	Morphine, moderate adverse events. Ketamine, moderate-severe adverse events. Gabapentin, adverse events similar to those reported in the control arm.
Fang et al. (2013)	Not specified	Not specified	Pharmacological interventions; antidepressants, anticonvulsants, opioid analgesics and tramadol, local anaesthetics and antiarrhythmics, NMDA receptor antagonists, NSAIDs, capsaicin, calcitonin, beta-adrenergic blockers, clonidine, skeletal muscle relaxants, emerging adjuvants, comparative and combined therapies.	Not specified.	Not specified.	Inconclusive, tricyclic antidepressants, gabapentin, tramadol, opioids, local anaesthetics and NMDA receptor antagonists may be beneficial.	The review did not report on adverse events of included studies.

McCormick et al. (2014)	Not specified	Not specified	Pharmacological interventions; sodium channel blockers, sodium channel blockers with opioid, neuromuscular transmission inhibition, antiepileptic's, opioids, hormonal, NMDA receptor antagonists.	Not specified.	Not specified.	Inconclusive for all pharmacological interventions. Perioperative IV ketamine and IV morphine may provide short term benefit. PO morphine may provide intermediate-long term treatment effect.	The review did not report on adverse events of included studies.
Deep brain stimulation							
Bittar et al. (2005)	424 (9) thalamic pain, PLP, stump pain, cervical root / brachial plexus lesion, failed back syndrome, peripheral / trigeminal neuropathy, post herpetic neuralgia, causalgia, cancer pain, anaesthesia dolorosa, SCI / paralysis, LBP, thoracic neuralgia, osteoporosis, post-operative pain, other pains.	Not specified	Deep brain stimulation. Electrode placement dependent of pain condition (periventricular gray, periaqueductal gray, internal capsule, sensory thalamus).	Not specified.	*Rating of pain intensity (VAS, grading protocol), complete or partial relief, dichotomous outcomes. Time points for collection of outcome measures ranged from 1-15y.	Positive for well selected patients with refractory chronic neuropathic or nociceptive pain. Positive for failed back surgery syndrome.	The review did not report on adverse events of included studies.
Graded motor imagery (GMI) / Mirror therapy							
Bowering et al. (2013)	169 (31) chronic pain following stroke, CRPS, PLP, BPAI.	Intervention when chronic pain condition > 3m.	GMI or at least one component of GMI practiced over 2-6w.	Usual physiotherapy care, nonsequential GMI, covered mirror program, bilateral hand movement, compare different active treatments.	Rating of pain intensity (VAS, NRS, categorical rating of pain), multidimensional score (MPQ, neuropathic pain scale) Time point for collection of outcomes measures, immediately post intervention.	Positive for GMI and mirror therapy. Negative for motor imagery.	Motor imagery may increase pain.

Rothgangel, Braun and Beurskens (2011)	344 (31) stroke, post stroke CRPS, CRPS, PLP, BPAI.	Varied; Average time post stroke 26.2d-4.9y, post stroke CRPS average duration 2.8m CRPS average duration 51w-14m, PLP average duration, 14m-not specified, average time post TBI 28.5m, average time post BPAI 6.75y.	Mirror therapy given for >2 interventions either alone or in combination with other treatment strategies.	Usual physiotherapy, covered mirror program, compare different active treatments, nonreflective or transparent mirror, direct observation of affected arm.	Measurements on the activity level in stroke patients and ratings of pain intensity in PLP and CRPS patients. Time point for collection of outcome measures post intervention and up to 6m post intervention.	Inconclusive due to quality of evidence. Mirror therapy may improve recovery of arm function post stroke. Evidence on use of mirror therapy for PLP or CRPS in low.	The review did not report on adverse events of included studies.
Timms and Carus 2015	199 (146) amputees, CRPS, BPAI, SCI, peripheral nerve injury.	Varied; mean time since amputation when specified 9y-21y. SCS intervention post 3y and 8y of PLP.	Mirror therapy: 1 intervention, 4-8w protocol, individualised protocol, 12w-6m unstructured protocol, GMI 6w protocol	Not specified.	Rating of pain intensity (VAS), multidimensional score (MPQ), mean % reduction of pain.	Positive for mirror therapy for PLP.	The review did not report on adverse events of included studies.
Cognitive and behavioural interventions							
van de Wetering et al. (2010)	546 (154) amputees with PLP, mixed conditions, SCI pain, other.	Varied; mean duration of pain when specified 6m-13.9y	Varied cognitive or behavioural techniques delivered individually or in group setting. Number of interventions 1-20 over 1d-30w.	Active control treatment, usual care.	Rating of pain intensity (VAS, categorical pain scales), pain unpleasantness scale, pain frequency, multidimensional pain scales (MPQ, PRI, BPI), performance scales, quality of life scales, other scales.	Inconclusive due to quality and quantity of evidence.	The review did not report on adverse events of included studies.

Key (outcome measures): SF-36, short form-36; MPQ, McGill pain questionnaire; VAS, visual analogue scale; NRS, numerical rating scale; verbal rating scale; PRI, pain ranking index; BPI, brief pain inventory. **Interventions:** NMDA, N-methyl-D-aspartate; GABA, gamma-aminobutyric acid; PCA, patient controlled analgesia; IV, intravenous; EMLA, eutectic mixture of local anaesthesia; TIVA, total intravenous anaesthesia; TENS, transcutaneous electrical nerve stimulation; SSRI, selective serotonin reuptake inhibitors; NSAID, Non-steroidal anti-inflammatory drugs; PO, oral; GMI, graded motor imagery. **Conditions:** PLP, phantom limb pain; PLS, phantom limb sensations; SCI, spinal cord injury; LBP, low back pain; CRPS, complex regional pain syndrome; BPAI, brachial plexus avulsion injury. **Other:** SCS, single case study; d, day; w, week; m, month; y, year.

Appendix 2.4 Published systematic review on the effectiveness of acupuncture for treating phantom limb syndrome

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Review article

The effectiveness of acupuncture/TENS for phantom limb syndrome. I: A systematic review of controlled clinical trials

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Abstract

Introduction: Phantom limb pain (PLP)/phantom limb sensation (PLS) is common in amputees and difficult to treat but either acupuncture or transcutaneous electrical nerve stimulation (TENS) may provide relief. A systematic review of controlled studies was carried out to explore clinical effectiveness, cost-effectiveness and adverse effects of these treatments on PLP/PLS.

Method: Literature searches were carried out using 18 databases (inception – February 2013). Reporting quality and risk of bias of controlled studies were assessed by independent reviewers.

Results: In two controlled studies, acupuncture significantly improved pain compared with usual care (visual analogue scale 0.17 ± 0.804 vs. 1.82 ± 1.919, $p < 0.05$; visual rating scale 1.45 ± 1.52 vs. 1.81 ± 2.22, p: not reported); two studies using TENS showed significant improvement in pain compared with sham TENS (pain rating index total $F(1.31) = 7.48$, $p < 0.01$; pain complain 0/12 vs. 7/12). One study showed better pain relief with TENS stimulation at stumps than stimulation on contralateral side. The reporting quality and methodological quality of controlled studies are critically discussed.

Conclusion: There is some evidence for the use of acupuncture and TENS for the treatment of PLP/PLS but insufficient high quality evidence is available. No studies evaluated cost effectiveness or adverse effects.

Keywords: Phantom limb pain; Phantom limb sensation; Phantom limb syndrome; Acupuncture; Transcutaneous electric nerve stimulation; Systematic review

Introduction

Phantom[2] limb pain (PLP) is the pain that results from where an amputated limb was previously located [1]. It is always positively associated with non-painful phantom phenomena/sensation, residual-limb pain/stump pain, and non-painful residual-limb phenomena/sensation [2]. These phantom complexes usually coexist and are difficult to separate [3] and affect up to 85% of amputees [3–7], with [3]phantom limb sensations (PLS) [8], experienced by most patients, followed by PLP and stump pain [5,6]. Extremely bothersome pain is thought to be experienced by 25% PLP sufferers, with depression closely linked [9].

The underlying mechanisms of this pathological pain requires further clarification. It is generally accepted that a series of neuropathic mechanisms are involved [10,11], including sensory cortical reorganization and adaptation within both peripheral [12,13] and central nervous systems [14–16] after amputation.

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[1] http://www.lsbu.ac.uk/.

[2] According to International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD 10), G54.6 represents PLP.

[3] G54.7 represents PLS.

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Physical factors or psychological factors may also affect the severity of the pain [3,17].

It is a condition that is difficult to treat, with few mechanism-based treatments, and only a few treatments with positive outcomes [18,19]. Conventional treatments include medications, anaesthetics, psychological interventions and, in severe cases, surgical revisions [3]. However, it is reported that less than 10% of patients receive lasting relief from prescribed medical treatments [20]. Most research has focused on conservative treatment – one survey claimed that non-surgical treatments were perceived more effective compared to surgical ones [19]. Opioids, ketamine, lidocaine, sensory discrimination training and TENS were suggested by Flor, as controlled studies demonstrated reduction in PLP [3]. However there is a general lack of controlled clinical trials.

Acupuncture has been shown to be effective for various chronic pain conditions [21–24]. Various studies have investigated the mechanism of acupuncture action in the central nervous system (CNS) [3,24–26]. It has been suggested that acupuncture evokes complex somatosensory sensations, which may modulate the cognitive and affective perception of pain [27]. These effects are mediated by the brain and extending CNS networks [25,26]. In Chinese medicine theory, 'Qi' and 'blood' runs throughout the body. PLP is believed to be a result of disturbance in segment meridians, which lead to Qi disorder and blood stagnation, and finally resulting in pain. A recent systematic review using English language databases evaluated the effectiveness of acupuncture treatment in the management of phantom limb syndrome, and indicated that acupuncture may have a positive effect on phantom limb symptom [28].

TENS is also commonly used as an effective treatment for various kinds of pain [4,29]. Significant improvements in several PLP case reports and case series have been reported, although the underlying mechanism has not been demonstrated [28,30,31]. Unfortunately, most acupuncture and TENS related studies (mostly surveys, case studies and reviews) were conducted in early 1980s, at a time when the recognition of neuroactive agents was inadequate. Halbert and colleagues conducted a systematic review in management of chronic and acute PLP and recommended the use of TENS in 2002 [18]. A Cochrane review aimed to evaluate the effectiveness of TENS for PLP and stump pain in adults in 2010, but failed to identify any relevant RCTs [32]. This systematic review aimed to explore the clinical effectiveness, cost-effectiveness and adverse effects of both acupuncture and TENS treatments on PLP, for the general population, by searching for controlled studies in English, Chinese and Korean databases.

Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed through all stages of the design, implementation, and reporting of this review [33]. The protocol has been registered: CRD42013003918 [34].

Data sources and search terms

The literature searches were carried out in 18 databases. The search included: MEDLINE via Pubmed, all Cochrane Library resources, CINAHL, AMED, PsycINFO, ScienceDirect, Index to Theses in English databases; and for Chinese databases; China National Knowledge Infrastructure (CNKI), VIP, Wanfang, Chinese BioMedical (CBM); and for Korean databases; Korean Studies Information Service (KISS), DBPIA, Korea Institute of Science and Technology Information, Research Information Service System (RISS), Korea Med, Korean Medical Database (KM base), Oriental Medicine Advanced Searching Integrated System (OASIS), and National Assembly Library. All databases were searched from their inception to February 2013 using the terms: 'phantom limb' or 'traumatic amputation', AND 'acupuncture' or 'TENS'. Additional search terms and strategies in different languages are listed in Appendix 1.

Study selection

Inclusion/exclusion criteria

Participants: Studies with patients in all age groups, with any causation, and any stage of PLP or PLS were included in this review. *Interventions*: Studies of ear, scalp, electro or body acupuncture; laser/catgut embedding along acupuncture points/meridians; TENS. Intervention was used as the sole treatment or as an adjunct to other treatments (if the control group also received the same concomitant treatment as the acupuncture group). *Comparisons*: Studies which measured the effects on phantom limb pain by comparing an intervention (mentioned above) with a placebo or sham, no treatment or usual care were included. *Outcome measures*: Primary: any form of pain measurement, patient reported improvement (proportion of improvement or cured); secondary: quality of life; mental conditions (anxiety, depression, sleep conditions); adverse effects; costs. *Study design*: Controlled trials were appraised and clinical characteristics extracted; *Language*: Published in English, Chinese, or Korean. *Date*: Publications from inception of to Feb 2013. *Publication status*: fully published articles.

Data selection and collection

Three authors (XH, AL, NR) reviewed the search terms and strategies; three authors (XH, GY and ML) screened and selected eligible papers. Disagreements were resolved through discussion with AL and JL to meet final consensus. Authors were not blinded to the authors' affiliations, journal of publication, or study results.

Data extraction

A spreadsheet identifying clinical characteristics of acupuncture and TENS was designed for this review. Data extracted included: authors, year published, study design, sample size; characteristics of amputation; characteristics of interventions – i.e. treatment procedure with location of intervention, TENS machine/electro acupuncture machine, acupuncture points, and

Table 1
Outcome data from included controlled trials on relevant outcome measures.

Study ref., Country, study type, sample size	Reason of amputation; time since amputation; location; patient's age; symptom(s)	Intervention Details of intervention	Control		Long term follow-up
Finsen et al. (1988) [38], Norway, nRCT, $N = 51$	Diabetes or atherosclerosis (no traumatic and re-amputation were included); N/A; Below/through knee; N/A; PLP	A: sham TENS with chlorpromazine TENS: 30 min, bid during the 2 first postoperative weeks, 2w, Tenzcare stimulator, low frequency (7 pulses at 100 Hz, 90 μs), increased amplitude until the patient complained discomfort; Chlorpromazine: 10 mg, tid. All patients received analgesics on demand.	B: sham TENS	C: active low frequency TENS	1 year
Katz and Melzack (1991) [39], Canada, nRCT (controlled crossover design), $N = 28$	Peripheral vascular disease (12); accident (9); arterial thrombosis (3); tumour (2); radiation damage (1); polio (1); N/A; A-E (2), B-E (1), A-K (16), B-W (9); 23–73 years, Mean: 52.8; 3 groups: group non-pain PLS (9), group PLP (11), group No-PL (8)	Auricular TENS: The outer ears Electronic Neurogar III stimulator, 10–30 volts, fixed resistance: 2000ohms, pulse rate: 4 Hz, pulse width: 100 μs (rate could be changed according to patients adaption), 3 consecutive 10 min periods/session, 2 sessions TENS and sham TENS for three groups of patients – group 1: with PLP, group 2: with non-painful PLS, group 3: amputee with no feelings of phantom limb.	*Placebo TENS* Patients were told that they were receiving the appropriate amount of current but they were not.		×
Liaw et al. (1994) [40], Tai wan, nRCT,	Most by traffic accidents and occupational injuries; T: <1w–6m, C: N/A; upper limbs (T: 9, C: 5), lower limbs (T: 15, C: 22), Bilateral (T: 1, C: 2)	Acu: CLS (ipsilateral for bilateral amputation) 30 min after De qi, qd/bid, 1–7 treatments	Usual care (medication and physical therapy)		×

Table 1 (*Continued*)

Study ref., Country, study type, sample size	Reason of amputation; time since amputation; location; patient's age; symptom(s)	Intervention Details of intervention	Control	Long term follow-up
$N=57$	T: 17–78, mean: 39.9, C: 18–76, mean: 46.1; PLP & SP	Usual care were given There were 3 groups (based on the time of receiving acu treatment after the onset of PLP). G1: within one week; G2: by the 2nd week; G3: 3w–6m		
Liao (2008) [41], China, RCT, $N=60$	N/A; 3–24m; Upper limbs (38), lower limbs (22) 16–57 PLP	TENS (CLS) 30 min, bid, 20 treatments/session, 5–7 d rest between sessions, 2 sessions KD-2A TENS, 100 μs, 10 Hz, current: to tolerant;	TENS (at stumps)	×
Yang (2010) [42], China, nRCT, $N=44$	Earthquake wound; N/A; Upper limbs (6), lower limbs (38), including four cases in both sides; 14–55 (median: 41.5); PLP	*Acu* (20 min, qd) + Rehab programme Scalp acu: DU16, DU24; Sensory area (not specified which area); Body acu: A Shi point, LI4, HT7, PC6, ST36, SP6, SR3, B preferred if appropriate. EA for A Shi point (discontinuous wave, 100 Hz); DU16 – reducing method, remove the needle after *De qi*; Other points – even reinforcing-reducing method 5 treatments/w, 3w/session, no. of sessions provided: not specified	Rehab programme: (1). Massage at stumps: 20 min, bid; (2). Muscle exercises: 10 min, qd; (3). Kerotherapy: 30–60 min, qd; (4). Psychological involvement: not specified;	3m SF-MPQ $p<0.05$

E: English; C: Chinese; m: month(s); N: number; w: week(s); min: minute; d: day(s); w: week(s); m: month(s); yr: year(s); min: minute(s); qd: once daily; bid: twice daily; tid: three times daily; M: mean; SD: standard deviation; *P*: p-value; MCPAS: McGill Comprehensive Pain Assessment Schedule; MPQ: McGill Pain Questionnaire; EPI: Eysenck Personality Inventory; BDI: Beck Depression Inventory; STAI-S/STAI-T: Spielberger State-Trait Anxiety Inventory; WRQ: Wesley Rigidity Questionnaire; MRS: Mood Rating Scale; SRS: Sleepiness Rating Scale; SF-MPQ (including: PRI: Pain Rating Index; VAS: Visual Analogue Scale; PPI: Present Pain Intensity; VRS: Verbal Rating Score; R: Right; L: Left; B: Both sides; ILS: Ipsilateral stimulation; CLS: contralateral stimulation; Rehab: Rehabilitation; Acu: acupuncture; N.B. Only the outcome measures relevant to the pre-arranged inclusion criteria are recorded.

Table 2
Criteria used to assign level of quality.

RCT

	Consort items reported	Risk of bias from Cochrane items
Very poor	Less than a third	6 or more
Poor	Less than 60%	5 and possible risk from 1 other
Good	Between a third and 50%	4 and possible risk from 1 other
Very good	More than 60%	3 or less from 1 other

nRCT

	Trend items reported	Downs and Black quality score
Very poor	Less than a third	Less than 33%
Poor	Between 30% and 41%	Between 20% and 50%
Good	Over 33%	Between 37% and 100%

frequency of intervention; baseline measure and follow up outcome measure with mean, standard deviation and *P*-value for different time periods; and other useful information for the specific study, such as the technique of a special acupuncture manipulation, findings with a specific pulse width of the TENS treatment, etc. Details of controlled trials are given in Table 1.

Reporting analysis and risk of bias assessment

Quality appraisal was conducted only for controlled studies. The Consolidated Standards of Reporting Trials (CONSORT) [35] and Transparent Reporting of Evaluations with Non-randomized Designs (TREND) checklists [36] were used for randomized controlled trials, and non-randomized controlled trials respectively. A score (yes = 1, no = 0, not relevant/partial = 0.5) was given for each question in the 2 checklists for each study. If the item was not available for the study (i.e. item 17b – if it is not necessary to have binary outcome measure), a score of 0.5 was given. A percentage (sum of the scores/number of questions) was generated to show the general quality of the individual studies.

Risk of bias was assessed using the Cochrane Collaboration tool for RCTs [37] and methodological quality was assessed using Downs and Black for nRCTs [38]. The studies were divided into levels of quality according to the combination of the scores (Table 2) Reporting and risk of bias were assessed independently by XH and ET (English papers), XH and GY (Chinese papers), and ML (Korean papers). Disagreements were resolved by consensus (AL, JL and NR). Data extraction was completed by XH. Where necessary, additional information was sought from study authors.

Summary measures and synthesis of results

Where possible, frequency data was extracted for the interventions: the duration, frequency and the style of interventions (including intervention techniques, important parameters for TENS equipment and electro acupuncture, mentioned '*de qi*'); the location of treatment (on body/scalp/ear acupoint or not; on contralateral side, or ipsilateral side, or both).

The authors planned to assess the heterogeneity of participants in sociodemographics, the reasons and levels of their amputation; interventions and comparisons, various outcomes measures and the follow up period of the measurements, as well as the post-operative period before patients received treatment. It was intended that for normally distributed data, mean difference, standardized mean differences, relative risk with 95% confidence intervals should be calculated.

If there was missing data or the data were analysed using an in appropriate test, the data would be reported separately. If a sufficient number of studies (at least 10 studies) were available, we would attempt to assess publication bias using a funnel plot or Egger's regress test. If the meta-analysis could not be carried out, a narrative description of included studies would be reported.

Additional analyses

Subgroup analyses were planned for measuring outcomes for patients' treatments on contralateral side or on amputation side, with electro acupuncture or not acupuncture only, and low or high frequency pulse width for TENS treatment if data permit. All relevant parameters were compared and with sensitivity analysed if the data were adequate.

Result

Study selection

An initial search identified 1005 potentially relevant studies and 877 were excluded by screening titles and abstracts (Fig. 1). The remaining 130 were retrieved and screened by reading full text. A total of five papers met the inclusion criteria – three nRCT from English databases: [39–41], two from Chinese databases: one RCT [42] and one nRCT [43]. No additional papers were identified from Korean databases.

Characteristics of included studies

The four nRCT and one RCT were published between 1988 and 2010 in Norway [39], Canada [40], Taiwan [41], and main land China [42,43]. Study characteristics of the 5 controlled studies are summarized in Table 1.Three evaluated the effectiveness of TENS on PLP [39,40,42], and two evaluated the effectiveness of acupuncture on PLP [41,43]. The sample size ranged from 28 to 60 (total 237), with reported age range from 14 to 78. Three studies reported the reasons of amputation: peripheral vascular disease, accident/earthquake, arterial thrombosis, tumour, radiation damage, and polio. The type of amputation varied, including upper extremity amputation, lower extremity amputation, and both single side and bilateral amputation.

Three studies [39,40,43] did not report when the amputation was carried out nor the duration of pain. The other 2 studies were in a range of 1w–6m [41], and 3–24m [42]. All of the 5 studies had similar duration of the intervention: 20–30 min per treatment session, once/twice a day, with various lengths of re-evaluation time point ranging from 10 min immediately after stimulation [40] to 1 year follow-up after surgery [39].

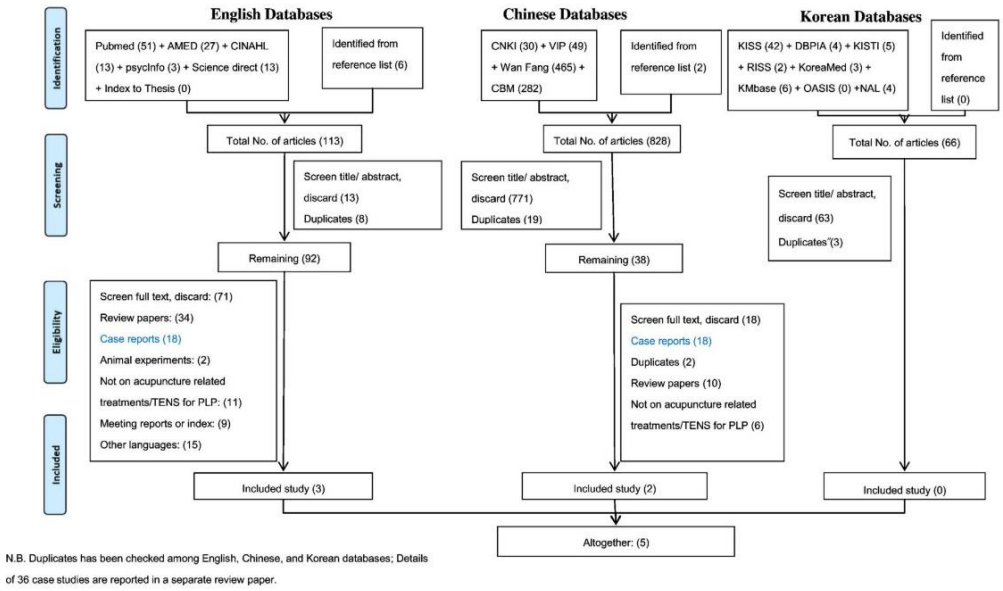

Fig. 1. PRISMA 2009 flow diagram.

Quality of reporting and risk of bias

Four nRCTs were quality appraised, of which two were of good quality (Downs and Black: 44% [40], 44% [43]; TREND: 45% [40], 45% [43]), and two of poor quality (Downs and Black: 33% [39], 37% [41]; TREND: 32% [39], 34% [41]). The RCT was very poor quality, with a very high risk of bias and a CONSORT score of 16% [42]. All five studies had written areas of inadequate reporting and the background information was limited (especially the two Chinese studies [42,43], with only one sentence introductions and no references). There were insufficient details on sampling, recruitment procedure and interventions for all the studies. The analyses were generally clear but limited. All five studies assessed outcome after the course of treatment, of which Yang [43] and Finsen [39] had follow-up at 3 months and one year respectively. None of the five studies presented sample size calculation, adverse effects, protocol or a registration information. The most common source of bias was the studies non-randomized design (the RCT had an inadequate description of randomization or blinding). Two of the five studies presented selective outcome reporting [42,43]. Only one study [40] presented both sociodemogaphic and condition similarity and clinical outcome baseline with $p > 0.05$ provided. In general, all 5 studies were deemed to have a high risk of bias and a low methodological quality.

Outcome measures

Pain was the most common outcome in included controlled studies. Only one study [40] evaluated mood, using Eysenck Personality Inventory (EPI), Beck Depression Inventory (BDI), Spielberger State-Trait Anxiety Inventories (STAI-S and STAI-T), Wesley Rigidity Questionnaire (WRQ), Mood Rating Scale (MRS), and Sleepiness Rating Scale (SRS). Outcome measures regarding pain included: Visual Analogue Scale (VAS), Verbal Rating Scale (VRS), McGill Comprehensive Pain Assessment Schedule (MCPAS), McGill Pain Questionnaire (MPQ) and Short-Form McGill Pain Questionnaire (SF-MPQ) (including: Pain Rating Index (PRI), VAS, Present Pain Intensity (PPI)).

Effects of interventions

Due to the inadequate data and heterogeneous nature of the outcome measures and interventions, it was not possible to pool the data. Full details of the studies are displayed in Table 1. A brief narrative description of the five included studies is reported below:

1. Acupuncture (+ usual care) versus usual care

   Two non-randomized controlled studies compared acupuncture with usual care [41,43]. Yang et al. [43] showed a combination of scalp/body/auricular acupuncture within a rehabilitation programme better improved PLP (after earthquake) (pain intensity on PRI, 1.12 ± 1.361 VS. 6.12 ± 5.892, $p < 0.05$; VAS, 0.17 ± 0.804 vs. 1.82 ± 1.919, $p < 0.05$; PPI, 0.19 ± 0.321 vs. 1.03 ± 1.318, $p < 0.05$) compared with the rehabilitation programme alone. This pain relief remained three months after follow up (PRI, 1.28 ± 1.436 vs. 6.84 ± 6.292, $p < 0.05$; VAS, 0.47 ± 1.724 vs. 2.05 ± 2.089, $p < 0.05$; PPI, 0.31 ± 0.864 vs. 1.33 ± 1.326, $p < 0.05$). Liaw et al. [41] showed that contralateral side (CLS) acupuncture relieved PLP and

may shorten the total period of suffering compared to usual care (medication and physical therapy), especially for patients given acupuncture within one week after onset of PLP: acupuncture received within one week: 1.45 ± 1.52; acupuncture received by the 2nd week: 1.75 ± 1.73; acupuncture received during three weeks to six months: 3.94 ± 2.86; control group: 1.81 ± 2.22. Baseline on Visual Rating Scale (VRS) of control group, and p values of final outcome of VRS were not reported. There were many inaccuracies with insufficient details provided in the tables and in the text. Authors were contacted for further details but no replies were obtained.

2. TENS versus sham TENS

   Katz and Melzack [40] showed that high intensity auricular TENS demonstrated significant reductions in the intensity of non-painful PLS (during bilateral ear stimulation period vs. initial: $F(1.69) = 4.26$, $p < 0.05$), as well as the pain level in PLP patients compared with sham TENS: post-session rating Pain Rating Index Sensory (PRI-S), $F(1.34) = 7.48$, $p < 0.01$; Pain Rating Index Total (PRI-T), $F(1.31) = 7.48$, $p < 0.01$). Mood rating: all $p > 0.05$, with no detailed data given.

   Finsen et al. [39] found that low frequency (2 Hz) segmental TENS reduced the analgesic dose needed: 1 week post-operation, mean (range): 5.5 (2–17); 2 week post-operation, mean (range): 2 (0–8); 3 week post-operation, mean (range): 0.5 (0–5); 4w post-operation, mean (range): 0 (0–7). It also provided analgesic relief: no patient complained of pain at 16 weeks post-operation, but 3/8 had recurrent pain at one year follow up. However, there was no baseline data available regarding analgesic dose, or the percentage of patients who complained of PLP and p values were not reported.

3. TENS at contralateral side versus TENS at stump

   Liao et al. [42] showed that the stimulation of the CLS of the amputation limb (especially when pain occurs) had a greater treatment effect in relieving pain compared with stimulation at stumps: VAS (right after treatment), 2.23 ± 2.24 vs. 5.77 ± 2.46, $p < 0.05$.

Discussion

In order to avoid overlapping in systematic reviews, existing reviews were first identified [33]. There was one systematic review [32] that evaluated TENS on PLP but only included controlled studies Another systematic review [28] published more recently explored the effectiveness of acupuncture for PLP, but only searched English databases.

Summary of evidence

All the selected studies recorded positive effects irrespective of the length of time PLP suggests that the intervention is likely to be beneficial irrespective of the length of time post-surgery that it is administered. However the quality of the RCT was very poor. Though there are two nRCTs of good quality, robust evidence could not be generated because of the nature of the study design.

Limitations

Due to the heterogeneity, lack of reporting and generally poor controlling of bias, results of effectiveness could not be combined. The quality of published controlled studies was limited; none of the studies scored more than 50%. The most common source of bias was the non-randomized design (or RCT with inadequate description of randomization or blinding), poor reporting of sampling, no protocol available, no sample size calculation, and no adverse effects reported. As the nature of nRCT can be subject to confounding factors, we are unable to draw definitive conclusions as to the effects of acupuncture or TENS on PLP/PLS. However, it is meaningful to include them as complementary approach of current evidence.

Although this review was unique as it included English, Chinese and Korean language papers, it did not include research in any other languages due to inadequate resources. However, including these three languages is likely to have captured the most relevant studies. A preliminary search suggested that a variety of acupuncture techniques were used in clinical practice for the treatment of PLP and that there was likely to be limited published research. In this review, a group of acupuncture related treatments were therefore considered; including TENS, acupuncture or acupoint/meridian based treatments (such as laser, catgut embedding). Meta-analysis could not be conducted because of the heterogeneous outcomes. There is also one deviation from the planned protocol as we planned to include systematic review in this review.

Implications

This review focussed on clinical effectiveness, cost effectiveness, and adverse effects of acupuncture/TENS for PLP. It has shown that acupuncture and TENS may improve pain and paresthesia, which are common clinical outcomes of PLP.

Further pragmatic randomized controlled trials evaluating the clinical effectiveness/efficacy, cost effectiveness, and adverse effects among acupuncture group compared with a sham acupuncture group, a TENS group compared with a sham TENS group are worthy of further exploration.

Further research studies should use appropriate guidance such as STRICTA or CONSORT and register, pre-designed protocols. More studies with large sample sizes and reliable and validated outcome measures are needed.

Conflicts of interest

All research was done by the authors. The authors do not have any conflicts of interest.

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Appendix 1. Search terms and strategies

	MeSH terms	Non MeSH terms	Chinese Databases	Korean Databases
1	Phantom Limb[a]	Phantom limb pain; phantom limb sensation;	Phantom limb pain [幻肢痛 / 断肢痛/幻肢痛/肢幻觉痛/幻肢症 / 截肢痛]	Phantom limb pain [환지통 /환상통]
2	Traumatic Amputation	Traumatic amputation amputatee	Traumatic amputation [创伤性截肢] Phantom limb [幻肢] Stump [残肢]	Traumatic amputation [절단]
AND				
3	Acupuncture	Acupuncture	Acupuncture [针灸/针刺], Electroacupuncture[电针], scalp acupuncture [头针], Ear acupuncture [耳针]	Acupuncture [침구/침자], Electroacupuncture [전침], scalp acupuncture [두 침], ear acupuncture [이 침]
	Acupuncture therapy Electroacupuncture Ear acupuncture	Electroacupuncture Ear/scalp acupuncture		
4	Transcutaneous electric nerve stimulation	Transcutaneous (electric) nerve stimulation	TENS [经皮神经电刺激/经皮电刺激], laser [激光], catgut embedding [埋线], [b]Rehabilitation[康复]	TENS [경피신경전기자극치료], laser [레이저/광선]
	Laser therapies	Laser acupuncture		

[a] 'Phantom limb pain(s)' and 'phantom sensation(s)' and 'pseudomelia(s)' comes under this heading.

[b] Search term of rehabilitation was included in Chinese study because many acupuncture related treatments are giving in rehabilitation department.

1– Medline via Pubmed search strategy (1950 – February 2013)
   1. (Phantom Limb[MeSH Terms]) OR traumatic amputation[MeSH Terms]
   2. (Acupuncture[MeSH Terms]) OR (acupuncture therapy[MeSH Terms]) OR (ear acupuncture[MeSH Terms]) OR (electroacupuncture[MeSH Terms]) OR (transcutaneous electric nerve stimulation[MeSH Terms]) OR (laser therapies[MeSH Terms])
   3. (#1) AND #2

2– AMED search strategy (1985 – February 2013)
   1. Acupuncture/or acupuncture.mp.
   2. Acupressure/or Acupuncture therapy/or acupuncture therapy.mp. or Ear acupuncture/
   3. 1 or 2
   4. Phantom limb/or phantom limb.mp. or Amputation/Amputation/or amputation.mp.
   5. Sensation disorders/or Phantom limb/or phantom limb pain.mp. or Amputation/
   6. Amputation/or amputee.mp.
   7. 4 or 5 or 6
   8. 3 and 7

3– CINAHL (all years)
   1. AB Phantom limb OR AB Phantom limb syndrome OR AB Amputee
   2. AB Acupuncture OR AB Electroacupuncture OR AB Transcutaneous electrical nerve stimulation OR AB laser
   3. 1 AND 2

4– psycInfo (1806 –Feb 2013)
   1. AB Phantom limb OR AB Phantom limb syndrome OR AB Amputee
   2. AB Acupuncture OR AB Electroacupuncture OR AB Transcutaneous electrical nerve stimulation OR AB laser
   3. 1 AND 2

5– ScienceDirect (all years)
   1. AB Phantom limb OR AB Phantom limb syndrome OR AB Amputee
   2. AB Acupuncture OR AB Electroacupuncture OR AB Transcutaneous electrical nerve stimulation OR AB laser
   3. 1 AND 2

6– Index to Thesis (all years)
   1. AB Phantom limb OR AB Phantom limb syndrome OR AB Amputee
   2. AB Acupuncture OR AB Electroacupuncture OR AB Transcutaneous electrical nerve stimulation OR AB laser
   3. 1 AND 2

7– CNKI (1915 – February 2013; key word; vague search terms; 武英文扩展检索)

(Acupuncture 针灸 OR Acupuncture 针刺 OR Electroacupuncture 电针 OR Scalp acupuncture 头针 OR Ear acupuncture 耳针 OR TENS 经皮电刺激 OR Laser 激光 OR Catgut embedding 埋线 OR Rehabilitation 康复) AND (Phantom

limb pain 断肢痛 OR 幻肢痛 OR 残肢 OR 肢幻觉痛 OR 幻肢症 OR 截肢痛 OR Phantom limb 幻肢 OR Traumatic amputation 创伤性截肢)

8– VIP (1989 – February 2013, abstract)
(Acupuncture 针灸 OR Acupuncture 针刺 OR Electroacupuncture 电针 OR Scalp acupuncture 头针 OR Ear acupuncture 耳针 OR TENS 经皮电刺激 OR Laser 激光 ORCatgut embedding 埋线 OR Rehabilitation 康复) AND (Phantom limb pain 断肢痛 OR 幻肢痛 OR 残肢 OR 肢幻觉痛 OR 幻肢症 OR 截肢痛 OR Phantom limb 幻肢 OR Traumatic amputation 创伤性截肢)

9– Wang Fang (1982 – February 2013, Title and abstract)
(Acupuncture 针灸 OR Acupuncture 针刺 OR Electroacupuncture 电针 OR Scalp acupuncture 头针 OR Ear acupuncture 耳针 OR TENS 经皮电刺激 OR Laser 激光 ORCatgut embedding 埋线 OR Rehabilitation 康复) AND (Phantom limb pain 断肢痛 OR 幻肢痛 OR 残肢 OR 肢幻觉痛 OR 幻肢症 OR 截肢痛 OR Phantom limb 幻肢 OR Traumatic amputation 创伤性截肢)

10– CBM (1978 – 20th February 2013, Title and abstract)
(Acupuncture 针灸 OR Acupuncture 针刺 OR Electroacupuncture 电针 OR Scalp acupuncture 头针 OR Ear acupuncture 耳针 OR TENS 经皮电刺激 OR Laser 激光 ORCatgut embedding 埋线 OR Rehabilitation 康复) AND (Phantom limb pain 断肢痛 OR 幻肢痛 OR 残肢 OR 肢幻觉痛 OR 幻肢症 OR 截肢痛 OR Phantom limb 幻肢 OR Traumatic amputation 创伤性截肢)

11– Korean studies Information Service System (KISS)(all years)
(Acupuncture 침 구 OR Acupuncture 침자 OR Electroacupuncture 전 침 OR Scalp acupuncture 두 침 OR Ear acupuncture 이 침 OR TENS 경피신 경전 기자 극치료 OR Laser 레 이 저 OR Laser 광선) AND (Phantom limb pain 환지통 OR Phantom limb pain 환상통 OR traumatic amputation 절단)

12– BPIA(1952 – February 2013; key word; vague search terms)
(Acupuncture 침 구 OR Acupuncture 침자 OR Electroacupuncture 전 침 OR Scalp acupuncture 두 침 OR Ear acupuncture 이 침 OR TENS 경피신 경전 기자 극치료 OR Laser 레 이 저 OR Laser 광선) AND (Phantom limb pain 환지통 OR Phantom limb pain 환상통 OR traumatic amputation 절단)

13– Korea Institute of Science and Technology Information (all years)
(Acupuncture 침 구 OR Acupuncture 침자 OR Electroacupuncture 전 침 OR Scalp acupuncture 두 침 OR Ear acupuncture 이 침 OR TENS 경피신 경전 기자 극치료 OR Laser 레 이 저 OR Laser 광선) AND (Phantom limb pain 환지통 OR Phantom limb pain 환상통 OR traumatic amputation 절단)

14– Research Information Service System (RISS)(all years)
(Acupuncture 침 구 OR Acupuncture 침자 OR Electroacupuncture 전 침 OR Scalp acupuncture 두 침 OR Ear acupuncture 이 침 OR TENS 경피신 경전 기자 극치료 OR Laser 레 이 저 OR Laser광선) AND (Phantom limb pain 환지통 OR Phantom limb pain 환상통 OR traumatic amputation 절단)

15– Korea Med(all years)
(Acupuncture OR Electroacupuncture OR Scalp acupuncture OR Ear acupuncture OR TENS OR Laser) AND (Phantom limb pain OR traumatic amputation)

16– Korean Medical Database (KM base) (all years)
(Acupuncture 침 구 OR Acupuncture 침자 OR Electroacupuncture 전 침 OR Scalp acupuncture 두 침 OR Ear acupuncture 이 침 OR TENS 경피신 경전 기자 극치료 OR Laser 레 이 저 OR Laser 광선) AND (Phantom limb pain 환지통 OR Phantom limb pain 환상통 OR traumatic amputation 절단)

17– Oriental Medicine Advanced Searching Integrated System (OASIS)(all years)
(Acupuncture 침 구 OR Acupuncture 침자 OR Electroacupuncture 전 침 OR Scalp acupuncture 두 침 OR Ear acupuncture 이 침 OR TENS 경피신 경전 기자 극치료 OR Laser 레 이 저 OR Laser광선) AND (Phantom limb pain 환지통 OR Phantom limb pain 환상통 OR traumatic amputation 절단)

18– National Assembly Library (all years)

(Acupuncture 침 구 OR Acupuncture 침자 OR Electroacupuncture 전 침 OR Scalp acupuncture 두 침 OR Ear acupuncture 이 침 OR TENS 경피신 경전 기자 극치료 OR Laser 레 이 저 OR Laser 광선) AND (Phantom limb pain 환지통 OR Phantom limb pain 환상통 OR traumatic amputation 절단)

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Appendix 2.5 Published narrative review on case studies using acupuncture to treat phantom limb syndrome

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Original article

The effectiveness of acupuncture or TENS for phantom limb syndrome. II: A narrative review of case studies

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Abstract

Introduction: Phantom limb pain and phantom limb sensation are extremely prevalent, affecting up to 85% of amputees, but with limited positive solutions available. Previous systematic reviews of complementary therapies suggested the use of acupuncture and transcutaneous electrical nerve stimulation. However, there is a lack of randomized controlled trials and inadequate information to guide clinical practice and future definitive research. This narrative review aims to provide guidance for using acupuncture or TENS and to identify potential outcome measures and optimum treatment protocols for clinical practice and future research.

Methods: Case studies identified in a previous systematic review were included, with clinical characteristics extracted to provide narrative description.

Results: Thirty-six case studies (257 individuals) were included. Acupuncture usually involved body needling and was most frequently reported on the contralateral limb. Chinese papers tended to use body and scalp acupuncture together; studies reported in English language journals tended to use one style. Acupoints along *Yang Ming* meridians, Liv 3, and LI 4 were commonly used. Needle retention time varied but was usually 30–40 min. Most Chinese studies reported daily treatment for 10–30 sessions, English studies tended to treat less frequently (weekly) and provide a smaller number of treatments (4–7 treatments). Contralateral stimulation in the upper fifth and middle 2/5 of sensory area were frequently used to activate lower limbs and body with scalp acupuncture. TENS treatment tended to be administered at the stump, the contralateral side and in relation to dermatomal pain patterns and innervating peripheral nerves. High frequency TENS was the most frequently used treatment, usually administered more than once daily. Both acupuncture and TENS recorded positive outcomes. Visual analogue scales, numerical pain rating scales, pain rating indices and present pain intensity were common outcome measures.

Conclusion: Treatment protocols can be drawn from the case studies for clinical practice but information is variable. Differences in clinical practice between studies published in Chinese and English may be due to different educational background, qualifications, cultural expectations, and differences in healthcare systems and policy. Further studies are recommended to develop standard treatment protocols for further randomized controlled trials.

Keywords: Phantom limb pain; Phantom limb sensation; Phantom limb syndrome; Acupuncture; Transcutaneous electric nerve stimulation; Case study; Clinical guidance

Introduction

Phantom limb symptom, which includes phantom limb pain (PLP) and phantom limb sensation (PLS), is a prevalent condition, affecting up to 85% of amputees [1–5]. It may affect amputees from a very early stage post operation [6], continuing to have long-term chronic effects [7,8].

There are limited positive solutions available for amputees. Previous systematic reviews have explored the use of preemptive

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epidurals, early regional nerve blocks, mechanical vibratory stimulation [9], transcutaneous electrical nerve stimulation (TENS) [10] (ref: part 1 systematic review), and acupuncture [11] (ref: part 1 systematic review). However there is a general lack of randomized controlled trials that provide useful evidence (ref: part 1 systematic review). Potential valuable information has been excluded in the process of screening papers when conducting systematic reviews, which could be of benefit in practice or in future research. In addition, unlike other conditions such as low back pain, there is no standard information or guidance for practitioners on using acupuncture for the treatment of PLP/PLS.

This narrative review aims to provide clinical guidance for the use of acupuncture or TENS for PLP/PLS and to identify optimum treatment guidance which could be used for clinical practice or in future research.

Method

In the comprehensive systematic review carried out, all studies mentioning PLP/PLS irrespective of their study design were included (ref: part 1 systematic review). The methodology of the systematic review and search terms are described in detail in the previous paper (ref: part 1 systematic review). The 36 case studies excluded from the previous systematic review are presented in this paper and were analyzed separately by two reviewers. Clinical characteristics were extracted including country of study, sample size, reasons for amputation, time since amputation, location of amputation, patient's age, symptom(s), intervention parameters, outcome measurements, and long term follow up.

The data extraction focused on the clinical application of acupuncture and TENS, rather than the outcome effectiveness, as single case studies are considered at the bottom of hierarchical evidence and the least likely to produce good evidence for practice [12].

A narrative description of clinical characteristics of included case studies is presented.

Results

Characteristics of the 36 case reports/series are given in Table 1 [13–49]. Among the 36 case report/series identified, 26 used acupuncture [13–15,17,18,21,23–25,27–36,38,39,41,43,45–47,49], eight TENS [19,20,22,26,37,40,44,48], and two used both (acupuncture and TENS) [16,42]. Eleven case series originated from China [16,23,33–36,41,42,45–48] and 14 case reports were published in English [13–15,17–21,25–28,38,39]. Sample sizes of case series ranged from 6 to 29. Most Chinese case studies discussed the mechanism of treatments provided, using traditional Chinese medical (TCM) theory and possible biomedical mechanisms, while case studies published in English tended to have more detail on the treatments provided.

Twenty-eight case reports/series reported the effectiveness of acupuncture in the treatment of PLP/PLS (including case series which included both TENS and acupuncture) [13–18,21,23–25,27–35,38,39,41–43,45–47,49]. These included 186 cases of which 33 were upper limb amputees, 77 lower limb and 76 where the amputation was insufficiently described. The causes of amputation were: 102 traumatic, 16 medical, 69 unknown (Lu [35] reported on 17 causes of amputation although only 16 were included in the case series). Age of amputees ranged from 12 to 79 years and time since amputation ranged from 1 day to 57 years.

Acupuncture treatment styles included body acupuncture (12/28), a mixture of scalp and body (5/28), auricular only (3/28), scalp only (3/28), not recorded (2/28), either TENS or body acupuncture (1/28), a mixture of scalp, auricular body and TENS (1/28), and press ring needles (a style of acupuncture which uses small needles which are usually retained post treatment) on the contralateral side (1/28). 13/28 case studies reported needling body points on the contralateral side, 3/28 the ipsilateral side and 2/28 the stump, 2/28 used central points (points near the spine), 7/28 used general body points, 5/28 did not specify body area needled. Of the case studies using scalp acupuncture 4/28 needled the contralateral side and 4/28 did not specify side used. None of the auricular case studies specified the side of body used. 3/28 case studies reported using electro-acupuncture and 1/28 moxibustion in conjunction with acupuncture.

Point choice varied between individual case reports. A total of 52 different body acupuncture points were recorded. Meridians most frequently used were the *Yang Ming* (large intestine/stomach meridian), with 19 of the 52 points used being on these meridians. Mode point used was Liv 3 which was used in 11 of the studies. LI 4 was used in nine studies and Sp 6 in seven. Of the three studies reporting on scalp acupuncture only, two used different styles of treatment (Yamamoto New Scalp Acupuncture and Chinese scalp acupuncture) and one did not specify treatment given. Two of the three studies reporting on auricular acupuncture only used a single point to affect a specific area of the body. Needle retention time varied from 30 s to 3–4 days with the majority of studies reporting 30–40 min duration.

The Chinese studies record total number of treatments ranging from 1 to 60 with mode number of cases reporting between 10 and 30 treatments. Five studies did not record the total number of treatments [16,23,29,41,47]. Treatment frequency was recorded as daily in the majority of papers. In the English reports, the total number of treatments ranged from 1 to multiple with the majority (7/15 cases) reporting 4–7 treatments. The frequency of treatment ranged from daily to every 2 weeks, treatment was most commonly reported as weekly (4 cases).

There were eight case reports/series on the effectiveness of TENS intervention in the treatment of PLP/PLS [19,20,26,37,40,44,48,50] and two on both TENS and acupuncture (as reported above) [16,42]. The eight TENS-only papers included 71 cases of which 10 were upper limb amputees, 37 lower limb and 22 unknown. Cause of amputation was trauma in 43 cases, medical in 16 cases and unknown cause in 12 cases. Age of amputees was reported for 7/8 cases who ranged from 5 to 87 years. Time since amputation ranged from <72 h post-surgery to 28 years, with a wide variation of time periods within this spectrum. Treatment consisted of TENS at locations including contralateral side (4) [19,22,26,44], the stump (3) [22,44,48],

Table 1
Characteristics of acupuncture and TENS in phantom limb syndrome – case reports/series.

Acupuncture						
Study ref; country; sample size	Reason for amputation; time since amputation; location; patient's age; symptom(s)	Intervention parameters			Outcomes	Long term follow-up
		Treatment provided; location	Frequency, treatment period and other information	Equipment settings		
10 case series						
Chen et al., 2009 [16]; China; $N=21$	Traumatic 10–20 d Transfemoral (5), transtibial (8), transhumeral (5), transradial (3) 18–65 PLP and PLS – did not specify who and how many had what type of pain	TCM acu group: both CLS and ILS i.e. LI4, LI11, LI14, LI5, LI10	*De qi*, 30 min, qd, 10 d a session, 10 d rest before the next session	EA parameters: G6805; sparse-tense wave; current intensity: to tolerant	SF-MPQ (PRI, PPI) PRI, PPI: $p<0.001$	×
		TENS group: ILS	20 min, qd-bid, 10 treatments a session, 10 d rest before the next session	TENS parameters: 1–10 Hz; pulse width: 150–500 μs; current intensity: to tolerant		
Wang et al., 2004 [42]; China; $N=13$	Accident 1–6 m (mean: 2.5 m) Transfemoral (7), transtibial (3), transhumeral (2), transradial (1) 18–48 (mean: 34) PLP (with description of the properties of pain)	TCM acu main points: LI4, PC6, ST36, SP10 Upper limb pain: scalp: CLS sensory area – middle 2/5; body: Jia Ji points – C4-7 Lower limb pain: scalp: CLS sensory area – upper1/5; body: Jia Ji Points – L1-5 Adjunct points: amputee side Upper limb: LI15, LI11, SJ5, LU5, LI10, SJ3 Lower limb: ST31, GB31, ST32, GB34, GB39, BL60, LR3, KI1	All treatments provided for 30 d 1 st stage: 20 min *Jia Ji Point* EA (+ GB30 if it is lower limb pain); 2nd stage: 20 min other points (EA on main points) 40 min/treatment, qd	EA (for *Jia Ji Points*) parameters: 6805-A, continuous wave, 200 times/min; current intensity: to tolerant	VAS, SDS: $p<0.01$	×
		TENS: at stumps	20 min, qd	KD-2 A; two-way asymmetrical square-wave current; 100 Hz; 100 μs; break output (2 s, 2 s); current intensity: to motion threshold		
		Other treatments include: Medication: 25 mg, po, bid; carbamazepine 0.1 g,po, tid Kerotherapy; exercises and psychological input	Thermotherapy: 20 min, qd; exercise: 30 min, qd; psychological input: 10d a session for 3 sessions	Thermotherapy: 50–55 °C		

Table 1 (*Continued*)

Acupuncture						
Study ref; country; sample size	Reason for amputation; time since amputation; location; patient's age; symptom(s)	Intervention parameters			Outcomes	Long term follow-up
		Treatment provided; location	Frequency, treatment period and other information	Equipment settings		
Yang, 2004 [47]; China; *N* = 29	N/A 3 d–> 20 years N/A 21–74 Stump pain (22), PLP (7)	Scalp acu: insert needle from DU20, direct to EX-HN1 in four directions Body acu: if upper limb – *Jia Ji point* T2, T3; if lower limb – *Jia Ji point* L2, L3 Psychological input was provided	30 min, 10 treatments/session, 1 d rest between sessions Scalp acu: 0.5–0.8 cun, even reinforcing-reducing method *Jia Ji point*: 0.5–1 cun, even reinforcing-reducing method; with manipulation several times (each time 5 min	N/A	1. Pain Stump pain: 54.6% cure – without any phantom limb symptoms after treatment; 31.8% showed effects – symptoms occur occasionally (especially when there is emotional/weather changes); 13.6% no effects – no change after treatment. PLP: 42.9% cure; 28.6% showed effects; 28.6% no effects. 2. Time since amputation ≤3 m: 61.6% cure; 33.3% showed effects; 5.6% no effects. >3 m: 36.4% cure; 27.3% showed effects; 36.4% no effects	×
Hu et al., 2003 [23]; China; *N* = 12	Accident (7) and TAO (2) 2–6 m (mean: 3 m) Transfemoral (5), transtibial (7) 21–55 (mean: 41.5) PLP	TCM acu: DU16, DU20 ST34, SP10, ST40, SP9, SP6, ST41, LR3 (manual even reinforcing-reducing manipulation or EA) Scalp acu: sensory area – upper 1/5 and Foot-motor sensory area Auricular: Brain and *Shen Men* Other treatments include: functional exercises, kerotherapy, and psychological input	DU16 and DU20 – *De qi*, then remove the needles Body acu: 20–30 min Scalp acu: rapid twisting, 200 times/min, 20–30 min or EA alternatively used Auricular: 30–60 min, qd, 2 ears alternatively	EA parameters: high frequency pulse current, 50–100 Hz, 10–15 min	Symptoms relieved by 50%: 66.7% by 20%: 25%; no improvement: 8.3%	×

Lu, 2002 [35]; China; $N = 16$	Accident (12), war wound (5) (did not explain why there were 16 patients altogether) 18–57 years Upper limb (4), transfemoral (3), transtibial (9) 52–78 PLP	TCM acu: principal: selecting points from the corresponding meridians Upper limb: HT1, LI15, SI9 Lower limb: BL36, LR11, ST31, or BL40, SP9, GB34	5 d/w, 10–15 sessions Using "Dao Qi Fa" – after De qi, lifting and thrusting gently. Better to feel the needling sensation at stumps or at distal parts of hand or foot	N/A	3 m follow up: General effective rate: 81.25% 56.25% – effective: PLP (severity, frequency and time) relieve by 80%, no pain killer 25% – improved: PLP (severity, frequency and time) relieve by 5% (probably it is a typo for 50%), the dosage of pain killer relieved by 50% 18.75% – no improvement: both PLP and the dosage of pain killer relieved less than 50%	3 m
Liu and Huang, 2001 [33]; China; $N = 23$	Accident (13), osteosarcoma (5), chronic osteomyelitis (3), gangrene (2) 1 month – 7 years N/A single limb (20), various limbs (3) 12–67 PLP (with description of the properties of pain)	Scalp catgut embedding: sensory area – upper limb: CLS middle area, lower limb: CLS upper area (not specified the proportion of upper/middle/lower area)	Once a month, 3 treatments/session, 1 session While embedding catgut, patients were asked to do flexion/extension exercise with their amputation limb. Psychological interventions were also given during this process	Needle length: 16 mm, catgut size and length: 0/4, upper limb: 4 cm, lower limb: 2 cm	Cure rate: 65.2%; 21.7% showed effects; 13.1% showed no effects 1 yr follow-up was reported for one case: no recurrence	1 yr
Wang et al., 2001 [41]; China; $N = 14$	N/A 4 d–7 years N/A 12–44 PLP	TCM acu: Main points: LI4, LR3, SP6 Adjunct points: (1). if transradial: add SJ5, LI10; (2). if transhumeral: LI15, LI14; (3) if only toe amputation: well points (not specified); (4) if transtibia: GB34, GB39; if transfemoral: ST31, ST32 Main points – B (preferably if possible) Adjunct points – CLS	15–30 min, qd, 10 d a session Treatment period: 10 d–4 w *De qi*, strong stimulation, reducing method No other medication involved during the treatment	5 *cun* needle – 0.35 × 125 mm	General effective rate: 100% Cure rate: 71.4% – no PLP after treatment and with a 2 years follow up 14.3% no PLP after treatment, recurred during 2 years follow up, but was relieved after further treatments 14.3% PLP relieved after treatment, but got occasionally PLP 2 yrs follow-up was reported for one case: no recurrence	2 yrs

Table 1 (*Continued*)

Acupuncture						
Study ref; country; sample size	Reason for amputation; time since amputation; location; patient's age; symptom(s)	Intervention parameters			Outcomes	Long term follow-up
		Treatment provided; location	Frequency, treatment period and other information	Equipment settings		
Liu, 1999 [34]; China; $N = 10$	PLP Other information was not reported	TCM acu: Group A: CLS, if both feet amputeed, points in hands counterparts used Group B: LI4, LR3, HT7, PC6, ST36, SP6 Group C: ILS (2–3 needles) Three groups alternatively	De qi, 60 min; manipulate every 15 min, qd, 6 treatments/w Group A: reducing method for 2 min Group B: even reinforcing-reducing method Group C: strong stimulation, reducing method	N/A	Improvement (did not mention according to what criteria) >80% – 5 cases; >50% – 3 cases; >20–50% – 1 case; no improvement – 1 case	×
Luo, 1998 [36]; China; $N = 12$	N/A 1–7 d Upper limbs (8), lower limbs (4); 17–48 PLP	Scalp acu: sensory area – upper limb: middle area, lower limb: upper area (not specified the proportion of upper/middle/lower area) Body acu: Selecting points from the corresponding meridians; i.e. GB30 (ILS) Reducing manipulation	30 min, qd, 7 treatments/session, (period of treatment was not provided, in one example, 8 treatments were given)	N/A	No PLP recurrence with 3 m follow up: 7 cases No PLP after treatment but with occasionally recurrence: 3 cases; no PLP after treatment but always recur: 2 cases	3 m
Xing, 1994 (2 refs) [45,46]; China; $N = 15$	War wound (8)/femoral artery embolism (1)/tumour about knee (1)/accident (5) 3–49 years Lower limbs 60–79 Additional information: 2/15 patients got PLP for the whole amputation limb, 13/15 patients got PLP for partial of the amputation limb (1 pain in the heel, 12 digits pain) (with description of the properties of pain)	TCM acu: Group 1: Body acu – DU16, DU24, PC6, HT7, ST36, ST40, SP10, SP6, LR3 (Points in upper limb – B; points in lower limb – CLS) Group 2: Scalp acu: sensory area – upper 1/5 (CLS) Two groups were given alternatively Moxibustion was provided if patients felt cold (ILS)	Group 1: DU16 – *De qi*, 1 min manipulation, remove needle, then insert needles to other points; ST 36 – reinforcing, ST40 – reducing, other points – even reinforcing-reducing method 30 min, qd, 3–4 w Mentioned specification of the needles; and details of inserting technique	EA (only for scalp acu) parameters: WQ-1ODI, continuous wave, 200times/min, to tolerant, 30 min Moxibustion: bird-pecking moxibustion, to cause warm and flush at local site	General effective rate: 80% Symptoms disappeared completely: 3/15; relief by 50%: 5/15; by 20%: 4/15; no improvement: 3/15	×

18 case reports						
Davies, 2013 [17]; UK; $N = 1$	Crush injury and compartment syndrome because of overuse of drugs; 13 w; transhumeral lower-third (R); 45 PLP and PLS (with description of the properties of pain/sensation)	Acu: *De qi* 1st treatment: CLS: GB21, LI14, LI11, LI8, LI4 2nd treatment: LI4, LI11, LI8, LI4 Other intervention includes: medications (clonidine, diazepam, pregabalin, paracetamol, tramadol and venlafaxione)	1st treatment: 3 min, 2nd treatment: 5 min; weekly, 7 treatments	N/A	After 5 treatments: VAS in PLP: completely resolved from 73/100, VAS in PLS: 94/100 – 19/100 The patient injured 2 d before the 6th treatment. No PLP or PLS reported after the treatment 3 w follow-up: no PLP, VAS in PLS: 30/100; 19 w follow-up: no PLP, VAS in PLS: 7/100	3/19 w
Jiang and Qu, 2012 [24]; China; $N = 1$	Accident 4 yrs Transradial (L) 45 PLP (with description of the properties of pain)	TCM acu: Main points: "*Four Tian points*" (B) – SJ16, SI16, SI17, LI17 and *A-Shi point* (R) Adjunct points: DU20, DU23, SP10, ST36, LR3 (B); LI2, LI3, SJ2, SJ3 (R)	30 min, qd, 10 d/session, 6 sessions Using "*Dao Qi Fa*" – slow inserting and removing needles, using even reinforcing-reducing manipulation "*Four Tian points*"– De qi; SJ16, SI16, SI7 – small amplitude lifting and thrusting (100 times/min)	N/A	N/A The patient reported no PLP since, occasionally PLS Other information: with the acu needles specification	×
Kotlyar et al., 2012 [14]; Israel; $N = 1$	Traumatic 21 years Transfemoral lower-third (L) 59 PLP	Yamamoto new scalp acupuncture points were selected corresponded to the cranial nerves that matched meridians and brain points Mainly use: KI, BL, PC, GB, LI meridians	20 min, weekly, 35 treatments were given as of the writing	0.25 × 30 mm, silicon-covered, sterile acu needles	PLP intensity: 9 ± 1/10 to ~1 after 13 treatments, and remained at ~1 till the 35th treatments PLP duration: an average of 0.5 ± 0.25 min decrease after 16 treatments PLP frequency: reported a reduction of ~50% in the frequency after 24 treatments Sustained improvement in QoL	×

Table 1 (*Continued*)

Acupuncture						
Study ref; country; sample size	Reason for amputation; time since amputation; location; patient's age; symptom(s)	Intervention parameters			Outcomes	Long term follow-up
		Treatment provided; location	Frequency, treatment period and other information	Equipment settings		
Jacobs, 2010 [38]; US; $N=1$	Traumatic 16 w 4 limbs amputation: hip disarticulation (L), transfemoral (R), transradial (L), and transhumeral (R) 25 PLP in left hand (with description of the properties of pain)	Auricular laser acu: location N/A (L) Auricular needle acu: at cingulate gyrus (L) Other interventions include: oxycodone (rarely – not helpful), clonazepam (effective), massage, physical therapy, compression bandage, and a silver-based lining placed inside the compression bandage	1 session auricular laser acu, and 1 session auricular needle acu	Low-level laser device, output no more than 5 mW, frequency: 650 nm	0–10 intensity scale: Auricular laser acu: eliminated completely after 30 s, kept for 4 h before it increased to 5/10 again Auricular needle acu: 9/10 to 5/10 after 1 min stimulation and remained satisfied when asked on the next day	×
Fulton, 2010 [18]; US; $N=1$	Sarcoma 6 d Transpelvic 38 PLP and PLS (with description of the properties of pain/sensation)	Acu: CLS: LR3, ST36, SP6 B: LI4	20 min with 2 stimulations, 1 treatment	N/A	NRS in PLP: 7 to 0 (lasted for 3 h); relief of PLS (heaviness) the next day, allowing patient to use elbow crutches	×
Liang et al., 2007 [30]; China; $N=1$	Accident >30 yrs Transtibial (L) 50 PLP (with description of the properties of pain)	Scalp acu: MS8(R), MS6 upper 1/3 (R) Body acu: GB34 (R), GB39 (R), SP6 (R), LR3 (R), LI4 (B)	1 h, once the other day, 10 treatments a session, 3 sessions Scalp acupuncture: after insert 1 cun into subgaleal, manipulate for 2–3 min; during the 1 h treatment, manipulate twice (not including the 1 st manipulation after insertion) EA for body acu	*De qi* EA (for body acu): G6805 Dense wave 1 h, once the other day, 10 times/session, 3 sessions	N/A Pain relieving after one treatment; no pain after three treatments.	×

Zhang and He, 2006 [49]; China; $N=1$	Accident 1 yr Transtibia (R) 41 PLP (with description of the properties of pain)	TCM acu: GB30, BL36, LR3 (R) GB30, BL36 (L)	30–60 min, manipulate every 15 min, 2 sessions *De qi*, strong stimulation, reducing method	N/A	N/A Pain relief after one treatment, no pain after two treatments, no recurrence with 6 m follow-up	6 m
Hao and Hao, 2006 [21]; US; $N=1$	N/A Several months Both legs N/A PLP (with description of the properties of pain)	Scalp acu, no points specified Patient reported tingling and electricity-like sensation in his phantom toe during the treatment	1 treatment	N/A	PLP diminished considerably after 5 min treatment, and complete relief after 10 min treatment	×
Bradbrook, 2004 [15]; UK; $N=3$	Case 1: congenital bilateral talipes; 1 m (the most recent surgery); transtibial (L); 34 Case 2: Myeloma; 2 years; hemipelvectomy; 68 Case 3: Accident; 2 m; transfemoral (R); 19 All patients were with both PLP and PLS (with description of the properties of pain)	Acu: CLS LR3, SP6, ST36, ST37, ST32 5 acupuncture points were needled separately in turn (30 s each) Achieved *de qi*	Weekly Case 1: 4 sessions Case 2: 1 session Case 3: 4 sessions	LR3, SP6: 0.20 × 15 mm Seirin needles; ST36, ST37, ST32: 0.30 × 30 mm Seirin needles	Case 1: VAS in PLP: 9 to 2, VAS in PLS: 3 to 1 Case 2: VAS in PLP: 7 to 0, VAS in PLS: 5 to 0 Cases 1 and 2 were able to continue with prosthetic rehab Case 3: VAS in PLP: 8 to 3 after 1 session, back to 7 after 3 sessions, VAS in PLS: 6 to 2 after 1 session back to 8 after 3 sessions	2 cases were able to continue rehab
Li, 2003 [29]; China; $N=1$	Accident 3 m Transfemoral (L) 26 PLP (with description of the properties of pain)	Treatments provided: Physiotherapy, including audio frequency current therapy, magnet therapy, vibrational technique, acupuncture, biofeedback therapy, TENS, and exercises No other information was reported		N/A	Muscle strength test: 5-; RoM: hip extension 12°; left thigh circumference: 42 cm (no change); can walk 45 min with artificial limb; barthel index: 100; no PLP	×
Wang and Zhang, 1986 [43]; China; $N=2$	Case 1: Accident; 2 years, Transhumeral (R); 52 Case 2: Accident; not specified (found pain 7 d after amputation); transtibial; 16 Both cases had PLP and PLS (with description of the properties of pain/sensation)	TCM acu: Selecting points from the corresponding meridians (CLS) Case 1: LI11, LI14, SI3, LI15 Case 2: KI1, SP4, GB34	Qd, 7 treatments/session, 3 d rest between sessions, normally 2 sessions (Case 1: 4 treatments, Case 2: 5 treatments)	N/A	Case 1: PLP and PLS relief immediately after the 1st treatment, No PLP and occasionally PLS after 3/4 treatments; 3 m follow up: No PLP, PLS only when focused on it Case 2: PLP relief and felt relaxed in the amputation limb after the 1st treatment; relaxed in limb but PLP every 10 min during the 2nd treatment; occasional PLP, no PLS after 5 treatments; no PLP and no PLS after 6 m	3/6 m

Table 1 (*Continued*)

Acupuncture						
Study ref; country; sample size	Reason for amputation; time since amputation; location; patient's age; symptom(s)	Intervention parameters			Outcomes	Long term follow-up
		Treatment provided; location	Frequency, treatment period and other information	Equipment settings		
Aldrete and Ghaly, 1996 [13]; US; $N=1$	Industrial accident; N/A; hand (R); 40 PLP and SP	Seirin press ring acu At the CLS which patient experienced the most severe pain	Kept in place for 3/4 d	N/A	6 m follow-up: SP began to fade, analgesia duration: 12–16 h after needles came out 18 m follow-up: pain free for 10 m, occasional exacerbations of pain was treated with acu	6/18 m
Liaw et al., 1996 [31]; China; $N=1$	Accident; 2 w; transhumeral (L); 38 PLP and PLS	Acu: *De qi* CLS: LI4, Extra point – Yao Tiew, PC6, LI11 Bilateral: LV3, GB34	30 min, qd, 7 treatments	N/A	VAS after each treatment: 7.6, 5.3, 5.4, 5.0, 4.5, 3.6, 2.4 Brain blood flow: hyperfusion to the bilateral thalami and brain stem on the next morning following 2nd and 6th treatment	×
Johnson et al., 1992 [25]; UK; $N=1$	Traumatic head injury; 5 yrs; shoulder disarticulation (R); 47 PLP	5 separate treatments: (1). manual acu; (2). manual acu; (3) EA; (4). Acu-like TENS; (5). Manual acu 8 points (one at a time); needle was inserted 2 cm lateral to the cervical scar	30 min, 5 treatments during 2 w	EA: 15 Hz Acu-like TENS: 2.3 Hz – bursts of pulses, 80 Hz – pulse frequency	EEG recordings for the 1st 4 treatments, showed: duration of analgesia was brief, pain returned soon after removal of the needles Biochemical measurements for the 5th treatment, showed: no large changes paralleling the analgesia VAS decreased, $p<0.001$ (pre/post treatment mean)	×
Liu and Lou, 1990 [32]; China; $N=1$	Myeloma N/A Transtibial (R) 21 PLP in toe (R) (with description of the properties of pain)	Auricular acu: *Shen Men*, toe, and some other common used auricular points (no specific details)	One-off treatment Ask the patient to press and knead the points (5–10 min each time, 2–3 times daily)	Intradermal needle	No PLP after 3 d	×

Monga and Jaksic, 1981 [39]; Canada; $N=1$	Traumatic; 2 y; transradial (L); 36 PLP	Treatment 1–3: CLS: LI 4, LI 10, LI 11. Treatment 4–5: + CLS: PC 3, Lu 5, He 3, LI 12. Treatment 6+ including 10 daily treatments: +CLS: LI 14, LI 15 and electro stimulation added. Post 10 daily sessions: +ILS: LI 13, LI 14, LI 15. Long term management: TENS I: LI 13, LI 14, LI 15	First 3 treatments 20–30 min. Retention time not specified post this. Multiple treatments including 10 daily treatments	N/A	Prior to acupuncture unable to wear prosthesis due to pain. Post acupuncture able to wear prosthesis during the working day. 15 months post follow up amputee reported adequate pain control with weekly TENS usage and needed no medication	×
Levine, 1976 [28]; US; $N=1$	Traumatic 4.5 years 4 digits of hand (R) 47 Neuroma and PLP	Acu with electrical simulation and moxibustion, no points specified	4 treatments	50 Hz	Pain at start: 60% (0% – no pain, 100% – worst pain), relieved 50% on average; pain relieved gradually in 15 min and lasted less than 4 h. Persistent exacerbation of pain was reported after 4 treatments. The patient quit after 6 treatments	×
Leung and Spoerel, 1974 [27]; Canada; $N=1$	Traumatic N/A 2/3rds of thumb 59	Auricular acu: ILS: one point (not specified)	qd, 5 d	N/A	Instantaneous cessation of the entire pain syndrome, the stump could be freely palpated without any discomfort after 5 min With 5 d treatment: increased warmth feeling and a more normal skin sensation in the stump, pain did not return 3 m follow-up: sensitive stump but was able to use hand well	3 m

Table 1 (*Continued*)

TENS						
Author; year of publication; country; sample size	Reason for amputation; time since amputation; location; patient's age; symptom(s)	Intervention parameters			Outcomes	Long term follow-up
		Treatment provided; location	Frequency, treatment period and other information	Equipment settings		
5 case series						
Yuan et al., 2010 [48]; China; $N=24$	Injury following earthquake <72 h (5), >72 h (10); single upper limbs (6), single lower limbs (14), both lower limbs (2) 5–80 (median 33) PLP (not specify the no. of patients who had PLP)	Physiotherapy at stumps (TENS was provided if there was PLP) A integrated package of treatments were provided, including rehab programme, chiropractic, exercise, physiotherapy, occupational therapy and psychology involvement	TENS: 20 min, bid, 10 treatments a session	TENS: N/A	VAS, RoM, Barthel Index $p<0.05$ for the 3 outcome measures	×
Kawamura et al., 1997 [50]; Japan; $N=10$	Arteriosclerosis obliterans, malignant tumour, trauma 4 d–1.5 yrs Transfemoral (5), knee disarticulation (1), transtibial (2), transhumeral (2) Mean: 57 PLP	TENS: Chose the site with lowest VAS 4 cites: (1) at stumps; (2) CLS; (3) the skin over the spinous process corresponding to the dermatonal pain pattern; (4) forearm or leg: ILS.	30 min, tid, 9 w in average	Medtronic CO.M LTD., USA, square wave pulses, 225 microsecond pulse width, 20 pulses/s, intensity: 50–80 mA, 4 s stimulation followed by 2 s of resting	Before and after treatment (average 9 w): VAS: $p<0.001$; duration of pain: $p<0.01$; patients' perception: no PLP (4), 'excellent' reduced (5), 'good' reduced (1) 6 m follow-up: patients' perception: no PLP (5), mild PLP (5) 2 yrs follow-up: patients' perception: passed away (5), no PLP (3), mild PLP (2)	6 m, 2 yrs
Salim, 1997 [40]; Pakistan; $N=16$	6 victims, 10 traffic accident; 2–28 yrs; other information N/A PLP	TENS Painful trigger points or related peripheral nerves	30 min, qd for 2 w (was provided if needed)	100 Hz, 5–20 mA	All patients: 'opening cramp-like flexion' in their stump, pain intensity much reduced Most patients: no analgesics and tranquilizers	×

Winnem and Amundsen, 1982 [44]; Norway; $N=11$	Peripheral vascular disease (10), neoplastic bone disease (1); lower limbs; 37–87 PLP	TENS at stump and CLS (if two session of 5 consecutive days treatment were provided with no improvement)	15 min, bid, 5 consecutive d If poor response, another 5 consecutive days' treatment were provided If still no improvement, stimulating was given in CLS	1st consecutive d: 100 Hz at stump 2nd consecutive d: 2 Hz at stump; 3rd consecutive d: 100 Hz CLS, 4th consecutive d: 2 Hz CLS	Pain free (2), very definite improvement (5). No patients reported pain reappear at the pre-treatment level 3–12 m follow-up: The 7 patients reported decrease in analgesia consumption by 50%	3–12 m
Melzack, 1975 [37]; Canada; $N=6$	Stump pain (1), PLP (5) Other information was not given	Intensive transcutaneous electrical simulations NT (near trigger point) (3), IN (innervating peripheral nerve) (1), NA-DA (near trigger point/distant acupoint) (2)	20 min, treatment frequency and period varied (most received 1–3 stimulation sessions/w, some received bid on 4 successive days) Stimulations were carried out by many patients at home	Grass Model S8 stimulator, max output: 35 V (raising until claimed hurt) and 60 Hz (pulse rate were kept constant at 3 or 10 Hz), sine-wave, rates varied by the experimenter	Mean % decrease PPI: 62% Mean % decrease PRI: 55% 6–18 m follow-up: 32/53 patients were interviewed (not specify pain conditions). 66%: helped during the treatment 56%: pain reduced compare to before treatment started 50%: stimulation treatment produced long-term improvement.	6–18 m
3 case reports Giuffrida et al., 2010 [19]; UK; $N=2$	Accident; 12 m; transradial (L); 24; PLP (in left phantom hand), PLS, SP Viral infection (had accident 10 yrs before it); 23 m; transfemoral (R); 38; PLP (most painful points: top of shin just below knee, top of right foot – extensor digitorum brevis muscle area) (with description of the properties of pain), PLS	TENS: CLS limb – stimulation was given at the maximum pain point(s)	3 m	80 Hz, pulse width: 50, intensity: to patients feel strong, but not painful	Showed significant improvement but not completely eliminated 1 yr follow-up: maintain (patients' perception) Outcome measures: MPQ (pre-assessment), CPLP, GQPAA, VAS	1 yr

Table 1 (*Continued*)

TENS

Author; year of publication; country; sample size	Reason for amputation; time since amputation; location; patient's age; symptom(s)	Intervention parameters			Outcomes	Long term follow-up
		Treatment provided; location	Frequency, treatment period and other information	Equipment settings		
Katz et al., 1989 [26]; Canada; $N = 1$	Accident N/A Transfemoral lower-third (R) 23 PLS (both painful and non-painful)	TENS: CLS and outer ears	One session contained 7 consecutive periods of 9 min each (rest – baseline 1, contralateral leg stimulation, rest – baseline 2, bilateral ear stimulation, rest – baseline 3, combined, rest – baseline 4) 2 consecutive evenings (1st session: placebo TENS, 2nd session: TENS)	2-Channel Grass model S88 stimulator; outer ear: 4 Hz, 125 ms, 20–24 V;CLS: 100 Hz, 80 μs, 100–120 V	Phantom intensity: CLS showed significantly effective in decreasing the intensity of PLS compared with placebo; outer ears stimulation showed non-significant in increasing the intensity	×
Gyory, 1977 [20]; Australia; $N = 1$	War wound; approx. 3 w after the last operation; transradial (R); 28 SP	TENS: the same side upper arm and the rest of forearm	15–60 min, 3–4 times/d	<75 mA, pulse rate: 5–200/s, pulse duration: 0.05–5 ms, pulse width was adjusted to the most pain relief level, frequency: about 100 Hz (or to maximum response)	Pain free for 20 min after treatment No pain without the prosthesis and 20 min pain free with the prosthesis Pain relief for 2.25–4 h, no medication required 4 m after the last operation, the patient returned to work full-time	4 m after operation

E, English; C, Chinese; m, month(s); *N*, number; w, week(s); min, minute; d, day(s); w, week(s); m, month(s); yr, year(s); min, minute(s); qd, once daily; bid, twice daily; tid, three times daily; M, mean; SD, standard deviation; P, *p*-value; VAS, visual analogue scale; SDS, depressive self-rating scale; RoM, range of movement; NRS, numerical rating scale; (sf-)MPQ, (short form-) McGill Pain Questionnaire; PRI, pain rating index; PPI, present pain intensity; CPLP, Cambridge phantom limb profile; GQPAA, Groningen Questionnaire Problems after Arm Amputation; TAO, thromboangitis obliterans; cun, a variable unit of measure based on body size; MS, motor-sensory area; Acu, acupuncture; R, right; L, left; B, both sides; ILS, ipsilateral stimulation; CLS, contralateral stimulation; Rehab, rehabilitation.
N.B. In all cases, sham TENS refers to electrodes placed over relevant region, with inactive channel.

ipsilateral side (2) [20,22], trigger points/near trigger points (2) [37,40], related peripheral nerve (2), ear (1) [26], spinous process corresponding to dermatomal pain pattern (1) [22] and near trigger point/distant acupoints (1) [37]. Intervention parameters varied between case studies – three case studies used high frequency TENS [19,20,40], two high and low frequency TENS [37,44], one low frequency TENS [26] and two did not specify [22,48]. Duration of treatment was generally 20–30 min (4) [22,37,40,48] and ranged from 15 min to 60 min. One paper did not specify duration of treatment. Frequency of treatment ranged from 3–4 times daily (1) [20] to 1–3 times a week (1) [37]. Mode treatment frequency (5) [20,22,40,44,48] was more than once daily. One study [19] did not specify frequency of treatment. The total duration of treatments ranged from 2 days to 3 months.

Outcome measurements

Outcome measures that measured pain intensity using scales such as the visual analogue scale and numerical pain rating scale were recorded in 10 acupuncture papers [14–18,25,29,31,38,42] and four TENS papers [19,22,37,48]. Apart from pain intensity related outcome measures, functional status, mean percentage decrease in symptoms, biomedical measurements, blood brain flow, prosthesis usage and medication usage were also used as outcome measures.

Effects of interventions

Acupuncture

Eleven studies reported resolution of PLP [15,17,18,29,30,32,36,41,43,46,49], however PLS did not resolve in all these cases, three reported statistically significant improvement [16,25,42], three reported effectiveness rates: acupuncture was deemed 80% [46], 81.25% [35] and 100% [41] effective. Four studies reported the percentage of symptom relief: symptom relief varied from resolution of symptoms 71.4% [41], 65.2% [33], 42.9% [47], to no effect 28.6% [47], 13.1% [33] 0% [41]. Hu et al. [23] reported symptom relief by 50% in 66.7% of participants with 8.3% showing no improvement. One case series [34] reported 80% improvement ($n = 5/10$) to no improvement ($n = 1/10$) and one case series [36] reported ($n = 7/12$) resolution of symptoms. Six studies reported using specific validated pain outcome measures such as visual analogue scale (VAS) and numerical pain rating scale (NPRS) and three reported using a non-specific numerical pain score. Of these, six case studies showed an improvement of PLP/PLS of at least four out of ten points [14,15,17,18,31,38]. One case series showed an improvement of only one point (8–7/10) [15]. Two case studies reported increased prosthesis usage [29,39] and one reported termination of pain medication usage [39]. One case report reported aggravation of symptoms with acupuncture intervention [28]. Also, brain blood flow changes were noted post acupuncture in one case report [31].

TENS

PLP/PLS was reported as being statistically significantly reduced in four papers [19,26,48,50] and reduced or resolved in all other papers.

There were no studies evaluating the cost-effectiveness or adverse effects of treatment and little information was provided on the effect either for acupuncture or TENS on quality of life or mental health.

Discussion

Case series and case reports are regarded as being at a low level in the evidence hierarchy as they do not have a comparison or control group thus outcomes cannot be generalized [51].

It is unclear from these papers what the optimal acupuncture treatment is for PLP/PLS, and an optimal time to commence treatment was not apparent. The case studies suggested body acupuncture is the most commonly used approach for treating PLP/PLS. Chinese papers tended to use a mix of body and scalp acupuncture whereas English papers tended to use one style or another. Both methods have recorded positive outcomes. It is not clear whether scalp, auricular, body or a combination of these approaches is most effective for treating PLP/PLS. It is also unclear from the case studies when is the best time (how soon after surgery) to commence an acupuncture intervention. The selected studies used a variety of acupuncture points and favoured using points on the *Yang Ming* [阳明] meridians, which may be due to these meridians being considered rich in 'qi and blood' in TCM theory. *Yang Ming* meridians are frequently used for Wei Zheng [痿症] (neurological conditions such as cerebrovascular accident (CVA) which cause flaccidity, paralysis or muscle atrophy). Liv 3 (Tai Chong [太冲]) and LI 4 (He Gu [合谷]) were commonly used acupoints, possibly due to their pain relieving properties. These points when used in combination are called four gates and are commonly used to relieve general pain [52]. This may explain the wide variety of acupuncture approaches taken in case studies. Needle retention time varied but with the majority of studies reporting 30–40 min duration. Most Chinese studies record total number of treatments ranging from 10 to 30, with the majority of papers reporting daily treatment whereas English studies tended to treat less frequently (weekly) and provided a smaller number of overall treatments (4–7 treatments). This may be due to different educational backgrounds or qualifications, cultural expectations, and differences in healthcare systems and policy. Most case studies did not use validated outcome measures but 12/36 used VAS/NPRS/pain rating index (PRI)/present pain intensity (PPI) etc., making the results more robust.

The majority of papers used the contralateral limb for treatment. Contralateral needling was suggested thousand years ago in the classical Chinese Medicine text The Su wen [素問], also known as Basic Questions [53]. This text recommends – "*Ju ci* [巨刺], (contralateral needling) needling the meridian points; right for left, left for right" and "*Miu ci*" [繆刺], (acupuncturing the opposite superficial luo acupuncture points); right for left, left for right". These two methods are mainly given for pain

caused by qi stagnation and blood stasis, which fits with the theoretical understanding of PLP/PLS.

Case studies using scalp acupuncture also frequently used the contralateral side for treatment. Sensory nerves ascending to the cerebrum from the spinal cord cross from one side to the other in the medulla oblongata and in the spinal cord and sensory information is processed in the opposite side of the brain [54]. It has been suggested that lower limb sensory impulses reflect the upper and interior region of contralateral hemisphere posterior and central gyrus [46]. Therefore, CLS is also conducted in scalp acupuncture – to stimulate the contralateral side in the upper fifth of sensory area to active lower limbs and body [33,36,45,46]; and to stimulate middle 2/5 for upper limbs [33,36]. Anatomically could explain why the contralateral side is used in scalp acupuncture.

A variety of different methods used to apply TENS were used in the case studies, including different locations of application and the use of high and low TENS. All methods reported positive outcomes, suggesting TENS has a place in the treatment of PLP/PLS, but, as with acupuncture, there is no recommended standard method for treatment. Most cases reported TENS stimulation in the contralateral side, and with a preference of high frequencies.

However, it is unclear from the case studies whether best treatment should include treatment on the contralateral or ipsilateral side, at the spinous process corresponding to the dermatonal level or auricularly or a combination of the above. It is not clear from the case studies at what settings (frequency/intensity etc.) TENS should be applied or whether high TENS or low TENS is more effective. One study suggested low frequency, long wave width, and pulse current TENS for pain relief [16].

Limitations

As the nature of case studies can be subject to confounding factors, we are unable to draw definitive conclusions as to the effects of acupuncture/TENS. This review only included studies published in English, Chinese and Korean databases but it is likely to have captured the most relevant studies. One case study on TENS for PLP was not accessible [55].

Implications

General treatment protocols can be drawn from the case reports/series for clinical practice. Acupuncture intervention usually involved body needling (not just scalp or auricular) and needling was most frequently reported on the contralateral limb. General body points were used and points on the *Yang Ming* meridians were frequently included. Adjunctive treatment such as electro acupuncture, moxibustion and cupping were infrequently used if at all. Needle retention time tended to be 30–40 min. TENS treatment tended to be administered at the stump, the contralateral side and in relation to dermatomal pain patterns and innervating peripheral nerves. High frequency TENS was most frequently used and treatment was usually administered more than once daily. Overall current literature is too varied and imprecise to help guide clinical practice. But there are potential indications of treatment components, some of which were commonly used and could be used to guide any future research. Specifically, trials are recommended to address the following areas; when is the optimal time to use acupuncture in PLP/PLS amputees, what style(s) is best to use (scalp/auricular/body), choice of acupuncture points and the type of stimulation (manual/electro). Other research questions include: is high, low, modulated, or another form of TENS best to use; what treatment protocol should be used (for example, electrode placement, the selection pulse width, pulse rate, treatment time, intensity of treatment); what is the optimal treatment frequency; and how many individual treatments should constitute a course of treatment.

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Conflicts of interest

All research was done by the authors. The authors do not have any conflicts of interest.

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Appendix 4.1 Published Delphi paper on developing an acupuncture protocol for the treatment of phantom limb syndrome

Original paper

Developing an acupuncture protocol for treating phantom limb pain: a Delphi consensus study

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ABSTRACT

Background Little is known about how a Traditional Chinese Medicine (TCM) approach could be used to treat phantom limb pain (PLP). There is currently no standard acupuncture protocol in the literature to treat this syndrome.

Objectives To achieve consensus among a group of acupuncture practitioners on the pathology and recommended treatment of PLP and devise an acupuncture protocol for the treatment of this condition.

Methods A classical Delphi approach was used using two parallel online Delphi studies. One study focused on participants with past experience of treating PLP (TPLP, n=7) and the other on practitioners with no past experience (NTPLP, n=16). Two hypothetical case studies were provided and participants were asked for responses on how they would treat these patients. Three rounds were included. Participants were also invited to rate and comment on the finalised protocol. Round 1 data were analysed using content analysis. In subsequent rounds an a priori criterion for defining consensus was set at ≤1.75 IQR. A group median of 5–6 was considered to mean 'agree'.

Results 19 participants completed all Delphi rounds (12 NTPLP, 7 TPLP). 108 NTPLP and 76 TPLP statements were generated and circulated in round 2; 53% of the NTPLP statements and 62% of the TPLP statements met consensus in round 2 and 45% of the NTPLP statements and 44% of the TPLP statements met consensus in round 3. Participants all agreed with the final protocol developed.

Conclusions The protocol developed does not claim to be best practice but provides a preliminary consensus from practitioners practising acupuncture for the treatment of PLP.

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INTRODUCTION

Silas Weir Mitchell (1829–1914) coined the term 'phantom limb syndrome', but the phenomenon was recorded medically prior to this by Ambroise Paré (1510–1590).[1] Currently, most literature tends to focus on two categories of amputation-related pain: phantom limb pain (PLP) and residual pain. Phantom sensations are non-painful sensations.[2] Both PLP and phantom sensations may exist simultaneously.[3]

The incidence of PLP in the UK has been estimated at 0.1 per 10 000 person-years,[4] and recent large surveys suggest 75% of amputees suffer PLP.[5] However, reports on the prevalence of PLP vary considerably, possibly due to differences in methodologies, time points of assessment, definition and cut-off values used for diagnosis and the study population.[6]

PLP involves multiple changes along the neuroaxis.[7] Peripheral mechanisms include formation of neuroma and ectopic discharge.[8] Noxious stimuli due to nerve injury sensitise central structures and cause central sensitisation, wind-up, long-term potentiation and expansion of receptive fields of the central neurons.[9] Central sensitisation is characterised by reduction of inhibitory processes, increased excitability of the dorsal horn neurons and structural changes at the central nerve endings.[10] Amputation alters neuronal activity in cortical and subcortical structures,[11] and changes and distortion occur in cortical maps.[9] Reorganisation of the somatosensory cortex occurs surrounding the area representing the deafferenated limb.[12] Cortical fields deprived of input shrink and the receptive field becomes smaller. Adjacent representations from non-denervated parts of the body then take over the cortical field.[9]

Evidence for the successful treatment of PLP is inconsistent. In the UK, common first-line treatments include amitriptyline, gabapentin and pregabalin.[4] However, the short-term and long-term effectiveness of

these treatments remains unclear, with gabapentin demonstrating a trend towards short-term analgesic efficacy and amitriptyline being ineffective.[13]

Acupuncture has been shown to be effective in the treatment of chronic pain conditions[14] but has not been well documented for treating PLP.[15] The style of acupuncture and point choice varies widely in the literature.[16]

Three main consensus approaches are recognised in health research: the Delphi method, nominal group technique and consensus development conference.[17] The Delphi technique has the advantage of not requiring face-to-face contact, so facilitating input from a wider group of participants.[18] It is well suited to research in which there is incomplete knowledge about a problem or phenomenon and works well when the goal of research is to improve understanding.[19 20] The Delphi technique was used in this study to gain agreement on acupuncture principles and to develop a protocol for the treatment of PLP which could be used in future trials and clinical practice.

METHODS

As a broad understanding of views on treatment was sought, participants both with and without previous experience in treating PLP were included in the study and two parallel surveys were run (past experience of treating PLP (TPLP) and no prior experience of treating PLP (NTPLP)). A classical Delphi approach using an open first round to facilitate the generation of ideas[21] was taken and delivered online. The study was approved by London South Bank University Research Ethics Committee in September 2013, piloted in October 2013, commenced in November 2013 and completed in March 2014.

Recruitment

Professional acupuncture associations (British Acupuncture Council, Association of Traditional Chinese Medicine and Acupuncture Association of Chartered Physiotherapists) and universities teaching acupuncture were provided with information about the study and asked to forward information to members/past students. Any participant who contacted the researcher about the study was provided with information. An email sent back by the participant was taken as consent to participate. Convenience and snowball sampling was used to capture as many participants as possible with past experience of treating PLP. Inclusion criteria included: completion of recognised training in acupuncture, registered with a professional body, at least 3 years clinical experience, and the ability to communicate in English. With Delphi studies it is recommended that, for a homogeneous sample, a small sample size is appropriate, such as 10–15[20] or 8–12 participants,[21] and the study aimed to recruit approximately this number in each group.

Procedure

The study was quasi-anonymous (the principal researcher (ET) knew which response came from which participant but participants did not). An a priori criterion of three rounds of Delphi was set. A fourth anonymous round was included involving rating and commenting on the finalised protocol. Participants were asked to respond to each round within 7–10 days and each round closed after 2 weeks. Subsequent rounds were sent out 2 weeks after closure of the previous round. All questionnaires were developed using the Bristol Online Survey (http://www.survey.bris.ac.uk).

Round 1 questionnaire consisted of two hypothetical case studies and 12 open-ended questions per case. Rounds 2 and 3 included statements generated from analysis of round 1. A 'no comment' option was provided if participants did not feel qualified to rank a statement. Statements were ranked on a 6-point Likert scale (from strongly disagree to strongly agree). Round 3 also provided additional information: response from the last round, median and IQR. To minimise participant fatigue, questions for which ≥50% of the ranked statements had met consensus in round 2 were not included in round 3 unless agreement had not been met.

Analysis of data

Qualitative data were analysed using NVIVO 10 and quantitative data using SPSS V.21. In round 1 qualitative content analysis was used, using thematic criteria.[22] Raw data were condensed, and grouped and condensed statements which only appeared once were excluded from round 2. Two researchers (ET and NR) discussed and reviewed the grouped statements to ensure meaning was not lost or biased through researcher interpretation. A consistency check of coding was applied by testing intra-rater reliability 10–14 days after initial coding (ET). Inter-rater reliability was checked through a second coder (NR) who coded a portion of the data. In subsequent rounds an a priori criterion for defining consensus and agreement was set. A group median of 5–6 was considered to mean 'agree' and an IQR ≤1.75 was considered indicative of consensus.[23] Stability of results was assessed using a Wilcoxon matched pairs signed rank test. The results were deemed stable when there was no significant difference between items.[23] A p value ≤0.05 was used in this study. To maximise validity, SD was recorded to demonstrate convergence of results. Round 3 NTPLP and TPLP results were compared to allow for comparison and triangulation between groups.

RESULTS

Figure 1 shows participant flow throughout the Delphi process. A total of 37 practitioners initially expressed interest in participating; 23 completed round 1 (the

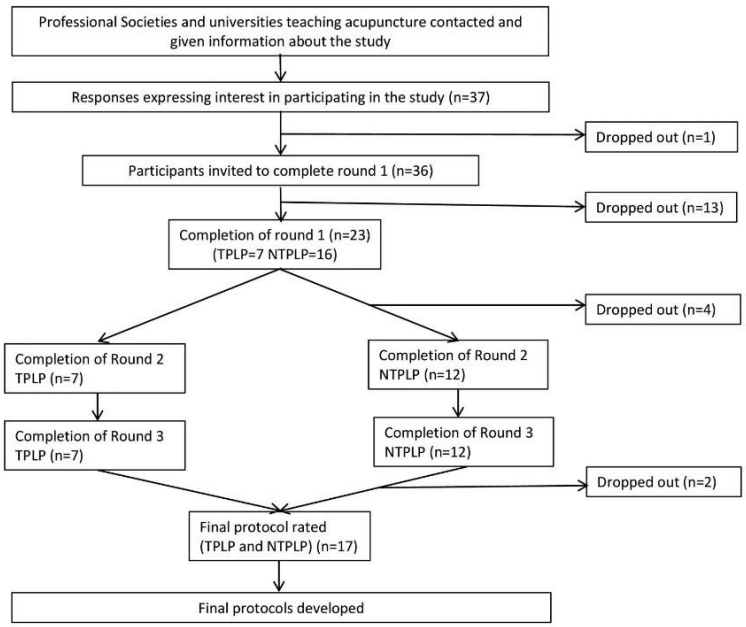

Figure 1 Flow chart of participants through the study. TPLP, practitioners with past experience of treating phantom limb pain; NTPLP, practitioners with no past experience of treating phantom limb pain.

TPLP group only managed to recruit seven participants), 19 completed both rounds 2 and 3 (12 acupuncturists, 6 physiotherapists practising acupuncture, 1 acupuncturist and physiotherapist) and 17 rated the final protocol. The reason for attrition by the 14 practitioners who did not complete round 1 was sought. A total of 12 responded with 7 reporting lack of time. Table 1 shows the demographics of the participants. All participants had completed acupuncture training in the UK; most practised a combination of Traditional Chinese Medicine (TCM) and 5 Element acupuncture. In the TPLP group, six practised TCM±other acupuncture styles and, in the NTPLP group, 12 practised TCM ±other acupuncture styles. Those who did not practise TCM practised Western medical acupuncture (n=5). In the TPLP group, six were acupuncturists±physiotherapists and one was a physiotherapist. In the NTPLP group, eight were acupuncturists and eight were physiotherapists.

Figure 2 provides data on the number of statements included in each round and the number of statements meeting consensus throughout the rounds. In round 1, 619 NTPLP statements and 292 TPLP statements were generated which were condensed down to 204 and 135 statements, respectively. Of the condensed statements, 96 were omitted in the NTPLP group as they did not meet the threshold for inclusion in round 2 (ie, only appeared once) and, in the TPLP group, 59 were omitted for the same reason. Of the statements included in round 2, 53% of NTPLP statements and 62% of TPLP statements met consensus and, in round 3, 45% of NTPLP statements and 44% of TPLP statements met consensus. The 'no comment' option was selected <21% of the time in the NTPLP group and <10% in the TPLP group.

Table 2 provides data on the questions which were included in round 3:13 questions in the NTPLP group and nine in the TPLP group. After completion of round 3, statements had met consensus and agreement for 7/12 questions (both for case studies 1 and 2) in the NTPLP group and, in the TPLP group, statements had met consensus for 8/12 questions (case study 1) and 10/12 questions (case study 2). The Wilcoxon matched pairs signed rank test showed good stability of results with no significant difference between rounds in 93.02% of NTPLP statements and 97.22% of TPLP statements.

Details of the hypothetical case studies and statements which met consensus and agreement are provided in the online supplement.

Comparison of the NTPLP and TPLP statements showed that there were differences. The NTPLP group did not meet consensus on whether to treat using body acupuncture or body and auricular acupuncture and whether to treat the contralateral or both lower limbs. The TPLP group, however, achieved

Table 1 Participant demographic data

Participant demographics	(n=23)	TPLP (n=7)	NTPLP (n=16)
Age			
31–40 years	3	0	3
41–50 years	10	4	6
51+years	10	3	7
Gender			
Men	8	4	4
Women	15	3	12
Professional background			
Acupuncturist	13	5	8
Physiotherapist practicing acupuncture	9	1	8
Physiotherapist and TCM acupuncturist	1	1	0
Professional membership			
BAcC	12	5	7
CSP (and AACP)	9 (5)	1 (1)	8 (4)
BMAS	1*	1	0
Australian natural therapists association	1	0	1
Place of study			
UK	20	5	15
UK and China	3	2	1
Years in practice			
0–5 years	5	0	5
6–10 years	3	0	3
11–20 years	11	5	6
21+ years	4	2	2
Current time in clinical practice			
PT	14	2	12
FT	9	5	4
Area of speciality			
Yes	16	5	11
No	7	2	5
Style of acupuncture used			
TCM	18	6	12
Western medical acupuncture	12	3	9
5 Element acupuncture	9	3	6
Japanese acupuncture	2	0	2
Battlefield acupuncture	1	0	1
Korean hand therapy	1	0	1
Other	1	1	0
Past experience treating PLSd			
Yes	7	7	0
No	16	0	16

Area of speciality refers to practitioners who have a specialist field (eg, pain management or treatment of infertility).
*The BMAS practitioner was a charted physiotherapist and TCM acupuncturist.
AACP, Acupuncture Association of Chartered Physiotherapists; BAcC, British Acupuncture Council; BMAS, British Medical Acupuncture Society; CSP, Chartered Society of Physiotherapy; FT, full time; NTPLP, participants with no past experience of treating phantom limb pain; PT, part time; TCM, Traditional Chinese Medicine; TPLP, participants with past experience of treating phantom limb pain; PLSd, phantom limb syndrome.

consensus on using auricular and body acupuncture on the contralateral limb. Additionally, the NTPLP group specified the acupuncture points: GV20, SP10, Four gates (a term for the bilateral point combination LR3 and LI4) and points on the lower back, taking a segmental approach to dermatomal pain (see final protocol, figure 3).

The study achieved consensus in nine of the 12 questions across case studies on the pathology and recommended treatment of PLP. By combining the four case studies and identifying similarities between cases, a protocol was developed (figure 3). Statements which appeared across case studies were included in the final protocol (see online supplement for the final list of statements which met consensus and agreement). The final protocol was rated using a 6-point Likert scale (from 1=strongly disagree to 6=strongly agree); 76.5% of participants agreed with the protocol, 11.8% strongly agreed and the remaining 11.8% somewhat agreed (median 5, IQR 5–5).

Six participants provided feedback on the protocol. Feedback included that it was considered interesting and surprising that consensus was not met in all areas and that the protocol allowed room for manoeuvre. One participant stated that he/she would not use GV20 and another felt needle retention time was excessive. One participant felt using the point pair LI4 and LR3 bilaterally (Four gates) was problematic, and it was proposed that *Yintang* could be used to replace LR3 on the amputated limb. One participant felt the protocol should be referred to as guidelines. One participant took the protocol to a team meeting and feedback was that a protocol was not needed as each patient would present and should be treated as an individual.

DISCUSSION

The aim of the study was to achieve consensus among a group of acupuncture practitioners on the pathology and recommended treatment of PLP and to devise an acupuncture protocol for the treatment of this condition. Consensus was established in 9 of the 12 areas under investigation and a protocol developed. It is acknowledged that, due to the background of some participants in the study, the protocol does include some statements which are specific to the constructs of TCM. However, practitioners from a Western paradigm would still be able to use the protocol.

Across case studies, participants achieved consensus on the pathology diagnosed. A common item was 'Qi and blood stagnation' (stagnation of energy and the circulation of energy in the body). Similarly, for both case studies there was consensus on the treatment principle to 'move qi and blood' and 'resolve pain'. Historically, in TCM, physical trauma (such as

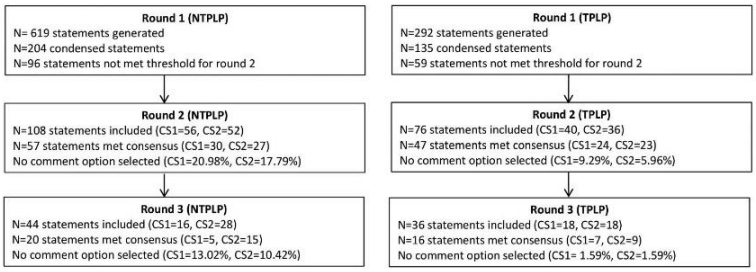

Figure 2 Number of statements generated and included in each round and number of statements meeting consensus in each round. CS1, case study 1; CS2, case study 2; NTPLP, practitioners with no past experience of treating phantom limb pain; TPLP, practitioners with past experience of treating phantom limb pain.

amputation) is referred to as 'causing the local stagnation of qi or blood', which causes pain[24] and this could be associated with peripheral pathology (such as the occurrence of neuroma and ectopic discharge) involved in PLP.

In this study the TPLP group reached consensus using a combination of body and auricular acupuncture. From a review of the literature, it is not clear whether auricular acupuncture, body acupuncture or a combination of these approaches is most efficient for treating PLP.[16] A systematic review suggests that auriculotherapy may be effective for the treatment of pain,[25] providing support for having auricular acupuncture within this protocol. *Shenmen* was the most commonly used point for the treatment of pain in a previous systematic review, which also supports its inclusion in this protocol.[25]

In keeping with this study, the acupuncture literature does tend to recommend treating the contralateral limb.[15 16] Treating painful conditions through the contralateral side is common practice in TCM.[26] Laboratory studies have compared the efficacy of ipsilateral and contralateral acupuncture and found that the degree of effectiveness is similar.[27 28] Clinical studies have found that both ipsilateral local needling and contralateral distal needling can reduce carpal tunnel syndrome.[29] Spinal interneurons may have an important role in reducing pain through contralateral needling.[30]

Specific body acupuncture points recommended in this study included LR3 and the Four gates (LR3 and LI4). These points are commonly used in case studies[16] and, in clinical practice, the Four gates are commonly used due to their calming effect and ability to treat pain.[24] The use of local acupuncture points may have met consensus because needling close to the injured tissue has the potential to elicit strong analgesic effects and encourage peripheral neuropeptide release (producing local vasodilation and modulating the local immune response).[31] Distal points which share innervation with the injured tissue or close to the spinal level that shares innervation with the injured part may have met consensus because they influence the segment via the dorsal rami.[31]

Consensus was met on advice to obtain *de qi* and to retain needles for 20–30 min. This was in keeping with acupuncture trials on treating PLP[15] and was not unexpected as many acupuncture textbooks recommend needle retention for this period of time.[32] In clinical practice, when treating elderly or constitutionally weak patients and depending on the style of acupuncture, needle retention time may vary. These possibilities may not have been addressed while developing this protocol.

No consensus was met on needle manipulation, possibly because needle manipulation can vary even between different acupuncture points within the same treatment depending on the intent of the practitioner and the specific function of each acupuncture point. No consensus was met on whether to use electroacupuncture or some other form of adjunctive treatment, and there was minimal convergence between rounds 2 and 3 with these statements. This may have been due to participants' familiarity with different treatment techniques and patient response to treatment. In the literature, adjunctive treatments are rarely used in conjunction with acupuncture to treat PLP.[16] In this study, consensus on treatment frequency and the total number of treatments was similar to UK case studies published on acupuncture treatment for PLP.[16]

The study had limitations. Consensus is a contentious component of Delphi studies. IQR is generally accepted as an objective and rigorous way of determining consensus and an IQR of ≤ 2 on a 10 unit scale or ≤ 1 on a 4–5 unit scale is considered a suitable indicator of consensus.[23] An IQR of ≤ 1.75 as used in this study may have been a slightly greater indicator of consensus but was chosen to avoid participant fatigue.

Also to avoid participant fatigue, not all statements were recirculated in round 3, meaning that the stability of the results could not be calculated for all items.

The protocol involved the opinion of both practitioners with (n=7) and without (n=16) past experience of treating PLP. Moreover, it is recognised that,

Table 2 Round 2 data on number of statements under each question which did and did not meet consensus and questions included in round 3

	NTPLP						TPLP					
	Number of statements met consensus		Number of statements not met consensus		Included in round 3 (Y/N)		Number of statements met consensus		Number of statements not met consensus		Included in round 3 (Y/N)	
Question	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2	CS 1	CS 2
1. What pathology/syndromes would you diagnose this patient with?	4	7	2	0	N	N	6	2	0	1	N	N
2. What would be your main treatment principle when treating this patient?	6	6	2	3	N	N	4	4	3	0	N	N
3. Would you use body, auricular or scalp acupuncture or a combination of any of these in the treatment of this patient?	0	0	2	2	Y	Y	1	1	0	0	N	N
4. If using body acupuncture, which limbs would you needle?	1	0	2	2	Y	Y	1	1	1	0	N	N
5a. What specific points would you use to treat the underlying pathology causing PLP in this case study and why (auricular)?	1	1	3	0	Y	N	3	4	0	0	N	N
5b. What specific points would you use to treat the underlying pathology causing PLP in this case study and why (body)?	12	7	4	8	N	Y	6	7	7	7	Y	Y†
6. Would you try and obtain *de qi* when needling this patient?	1	1	0	0	N	N	1	1	0	0	N	N
7. How long would you retain the needles for?	1	0	1	2	N	Y	0	1	2	0	Y	N
8. Would you manipulate the needles during treatment and, if so, how frequently?	0	1	4	1	Y	Y*	0	1	1	0	Y	N
9. Would you use electroacupuncture?	0	0	1	1	Y	Y	0	0	1	1	Y	Y
10. Would you use cupping, moxa or any other adjunctive treatment?	0	0	2	4	Y	Y	0	0	1	1	Y	Y
11. How often/frequently would you treat this patient?	2	3	1	1	N	N	1	0	0	2	N	Y
12. How many treatments would you anticipate giving in total for a course of treatment?	2	1	2	1	N	N	1	1	0	1	N	N
Total	30	27	26	25	–	–	24	23	16	13	–	–

*Included in next round as agreement not met (score ≥5).
†Included in next round as 50% not met consensus and researchers wanted clarity on consensus on point choice.CS1, case study 1; CS2, case study 2; NTPLP, practitioners with no past experience of treating PLP; PLP, phantom limb pain; TPLP, practitioners with past experience of treating PLP.

Underlying Pathology:	• Qi and Blood Stagnation (swelling and haematoma) • Pathologies specific to the individual (as diagnosed during assessment)
Main Treatment Principles:	• Manage and reduce pain • Move qi and blood • Treat pathologies diagnosed during assessment which are specific to the individual • Reduce stress and calm the mind if necessary
Style of Acupuncture:	• Combination of body and auricular acupuncture
Limbs Needled:	• Opposite limb to amputation and possibly also the residual limb
Recommended Auricular Acupuncture Points:	• Shenmen (to calm the mind and reduce pain) • Sympathetic (to manage stress and anxiety) • Points corresponding to the lower limb
Recommended Body Acupuncture Points:	• Local points on the stump depending on the health of the tissue and the patients reaction • Mirroring local and distal points by needling them on the opposite limb • Points on the lower back taking a segmental approach to dermatomal pain • 4 gates (LI4 + LR3) or LR3 (liver 3), • GV20 (governor vessel 20) (to lift the spirits, decrease stress and improve sleep), • SP10 (spleen 10)
Try and obtain deqi when needling:	• Yes
Needle retention time:	• 20-30 minutes
Needle manipulation during needle retention time:	• Consensus not met
Use electro-acupuncture:	• Consensus not met
Use of cupping, moxa or other adjunctive treatment:	• Consensus not met
Treatment frequency:	• Weekly or twice weekly and reduce frequency of treatment as symptoms abate
Total number of treatments:	• At least six (approximately 10)

Figure 3 Acupuncture protocol for the treatment of phantom limb pain.

although all practitioners were experienced, even those with past experience of treating PLP were not necessarily experts in this field. However, acupuncture is not commonly used for the treatment of PLP. In past surveys only 1% of amputees reported ever having used acupuncture.[33]

Professionals with both Western medical and traditional acupuncture backgrounds were included and therefore the protocol included a mixture of concepts. However, as the aim of this study was to capture a broad approach to treatment including expertise from different disciplines, this was not seen as a limitation to the study.

Potentially useful information was lost by introducing a threshold for inclusion of statements in round 2. However, due to the large number of statements generated in round 1, this process of reduction was deemed necessary.

This study elicited valid opinion from professional acupuncture practitioners. However, the Delphi technique does not produce right, wrong or definitive answers[21] and, although consensus was obtained and a protocol developed, it should not be interpreted as the best treatment approach.

This study did achieve consensus and develop an acupuncture protocol for the management of

phantom limb syndrome in lower limb amputees and practitioners' views on the pathology and treatment of PLP were established. The protocol developed in this study is novel and provides guidelines which have not been previously available for acupuncture treatment of PLP. The proposed protocol is not claiming to be the best or the most correct approach to treatment, but does give some guidelines for practitioners on which to base their treatment. The protocol allows practitioners to take a pragmatic approach to treatment which is in keeping with TCM while still providing a structure to treatment.

Further study is required to gain consensus on areas such as needle manipulation, the use of electroacupuncture and other adjunctive treatments and the use of channel pairing when mirroring points on the contralateral limb. This protocol will form the basis of a future randomised controlled trial being carried out by the authors.

Summary points

- Various acupuncture approaches are used to treat phantom limb pain and symptoms.
- We used Delphi consensus methods with (finally) 17 practitioners to devise a treatment protocol.
- The protocol is pragmatic but also consistent with a traditional approach.

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Contributors All authors were involved in the design of the study and analysis and interpretation of data. All authors reviewed and commented on the manuscript and gave final approval of the version to be published.

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Appendix 4.2 Published paper on Delphi methodology

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Research paper

Delphi methodology in health research: how to do it?☆

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ABSTRACT

Introduction: Delphi technique is widely used to develop consensus on group opinion. However, no strict guidelines exist and various methods are often employed. The aim of this article was to reflect on Delphi methodology and provide guidance useful to researchers in integrative medicine.
Methods: Two parallel Delphi studies were undertaken to achieve consensus on how to treat phantom limb pain with acupuncture. Whilst completing these studies methodological issues relating to Delphi technique were identified which may be of use to other researchers.
Results: Ten areas were identified;, use of the term 'expert', sample size and sample heterogeneity/homogeneity, iteration, structure of round one, optimal number of response categories, inclusion/exclusion of data in subsequent rounds, participant feedback, defining consensus, stability of response and agreement, attrition.
Conclusions: Defining and using the term 'expert' is problematic. Three rounds are optimal. Round one data collection and analysis need structuring to avoid generation of unmanageable amounts of data. Subsequent rounds should consider using Likert Scales with four to seven categories, with even number of categories eliminating the problems associated with midpoints. To ensure rigour, data should not be excluded from round three. Participant feedback should include both central tendency and a measure of dispersion and be presented graphically. Consensus should be clearly defined and not confused with stability of response or agreement. Attrition can be minimised by ensuring participants are well informed and through a short time frame between rounds. It is intended that this guidance may help future researchers.

1. Introduction

The Delphi technique is now a widely used methodology which has the advantage over other consensus methods of not requiring face to face contact [1] whilst still guiding group opinion [2]. It can facilitate wider group participation than other consensus techniques (such as nominal group technique and consensus development conference) so avoiding recruitment bias due to participants geographical location.

Delphi technique evolved due to limitations of traditional methods used to gain group opinion for policy development [3] and was founded on the premise that unstructured, face to face group predictions were weaker than individual statistical predictions [4] The original Delphi method was developed in the 1950's by Olaf Helmer, Norman Dalkey and Nicholas Rescher of the Rand Corporation to forecast the impact of technology on warfare [4]. It has subsequently been used in healthcare, marketing, education, information systems, transportation engineering [5] and complementary and alternative medicine (CAM) to establish guidelines and establish key components of an intervention [6,7,8].

Delphi technique is defined by its use of 'experts', and its use of a series of questionnaires interspersed with controlled feedback and provides information on group opinion [5]. It is an appropriate methodology when there is lack of agreement, incomplete knowledge, uncertainty or lack of evidence [9]. This technique does not intend to challenge statistical or model based procedures but instead is intended for use in situations where statistical methods are not practical or possible [5].

Delphi technique has four main characteristics; anonymity between participants, iteration with controlled feedback of group opinion, statistical aggregation of group response and expert input [3]. Anonymity allows views to be expressed and changed privately [5]. Iteration with controlled feedback allows 'communication' between participants and perspectives to be shared [9] and allows participants to change views [10]. Statistical aggregation of group responses allows for data to be analysed and interpreted [10].

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Expert input means each participant is informed in the area under study [11].

The aim of this article was to reflect on the Delphi technique as a research tool in healthcare. It draws upon a practical example from two studies carried out by the authors and highlights areas for consideration when using this technique [12]. The paper identifies a number of areas which need careful consideration, which could be useful for researchers when deciding whether to use this methodology and provides a list of the main issues (drawn from the above) to consider when using this technique (Table 1). The paper attempts to address areas not commonly considered in other reviews, such as what to consider when designing round one, the size of Likert scale, items to include in subsequent rounds and differentiating between consensus, agreement and reliability. The paper identifies areas needing consideration for the future use of the technique to inform integrative medicine research and provides a 'how to' guide.

2. Methods

In trying to achieve consensus from practitioners on how to treat phantom limb pain with acupuncture, two parallel quasi-anonymous studies were undertaken with a group of acupuncture practitioners both with and without previous experience of treating phantom limb pain [12]. Both studies used a Classical Delphi approach, (using an open first round to facilitate generation of ideas) administered online. One study included seven participants with past experience of treating phantom limb pain (PLP) (six acupuncturists ± physiotherapists and one physiotherapist) and the other 16 participants with no past experience of treating PLP (eight acupuncturists and eight physiotherapists). Two hypothetical case studies were provided and participants were asked twelve open-ended questions about the pathology and treatment of this condition. Subsequent rounds included statements generated from round one which participants ranked on a six point Likert scale. An a priori criterion of three rounds was set and participants were also asked to rate the protocol, developed from the Delphi study. Participants were asked to respond to each round within 7–10 days. First round data was qualitative and was analysed using qualitative content analysis. In subsequent rounds the data was quantitative and a group median of 5–6 was considered to mean agreement and an inter-quartile range (IQR) $\leq$1.75 was considered indicative of consensus. Wilcoxon matched pairs signed rank test was used to determine stability of results using a p value of $\leq$0.05.

3. Results

The data collected as part of this study and the resulting acupuncture protocol is reported elsewhere [12]. However, in summary, combining data from the two studies, nineteen participants completed all Delphi rounds (four dropped out). A

Table 1
Summary of areas to consider when designing a Delphi study.

Area of consideration	Recommendation
Expert panel	• Avoid labelling participants as 'experts' without consideration of the controversies of this label and the difficulties in defining 'experts'. • Be explicit about participant's expertise. • Recognise the limitations of Delphi studies (group consensus is not synonymous with 'best' or 'correct' results). • Consider the homogeneity or heterogeneity of the sample when deciding sample size.
Iteration	• Consider setting number of rounds *a priori*. • Three rounds of Delphi are optimal. • If developing a protocol, consider asking participants to rate the protocol post completion of the Delphi study.
Round 1	• Use few well-structured open-ended questions or a modified approach to develop initial statements. • Beware of generating large amounts of data for subsequent round.
Round 2	• Optimal number of response categories of the Likert scale lie between four to seven. • Consider the potential pitfalls of using a Likert scale with a midpoint. • Consider providing a 'no comment option' if participants have different backgrounds and knowledge.
Subsequent rounds	• Ideally recirculate all data from round two. • Be aware that omitting data can introduce bias and prevent full analysis of results.
Participant feedback	• Use both central tendency and a measure of dispersion to aggregate data (median and IQR). • Consider providing visual feedback (bar charts) to provide information on the distribution of data.
Consensus	• Define if consensus is being used to determine if agreement exists or as a stopping guideline. • Differentiate between stability, agreement and consensus. • A measurement of variance in response is appropriate for determining consensus.
Stability of response / internal validity	• Stability of response should not be confused with consensus. • If analysed, theWilcoxon matched-pairs signed rank test or ICC are appropriate methods to inferentially determine stability of response. Stability could also be determined though providing data on the median and IQR across rounds or through graphical representation.
Attrition	• Consider only recruiting participants with an interest in the topic. • Ensure participants are fully informed of the commitments of a Delphi study. • Ensure a short time frame between rounds to maintain participant interest and reduce attrition. • Ensure feedback is part of the agreement to take part.

Key: IQR, inter-quartile range; ICC, intraclass correlation coefficient.

total of 108 statements were generated from analysis of round one in the group with no past experience of treating PLP and a total of 76 statements were generated from the group with prior experience of treating PLP. In round two, across groups >50% of statements met consensus, and in round three >40%. All participants who rated the final protocol ($n = 17$) agreed with the final acupoint selection and treatment recommendations. Whilst completing the two Delphi studies, ten areas relating to this technique were identified as needing consideration (Table 2).

4. Discussion

4.1. The 'Expert' panel

Delphi uses non-probability sampling to recruit participants or create an 'expert panel' [11]. However the term 'expert' is contentious. Expert has been defined as 'informed individuals', 'specialists', and those with knowledge about a specific subject [11]. Experts are required to have; experience and knowledge of the issue being investigated, willingness and capacity to participate, time to participate and adequate communication skills [10]. However, within this criterion, there is debate as to how to define knowledge and experience. Although knowledge could be assumed through a professional qualification or registration, this does not ensure expertise. Equally so, expertise cannot be ensured though number of years in practice [13].

Although many authors recognise the difficulties of labelling participants as experts [11] this term is still used in CAM Delphi studies, with often very different criteria used to define this term [7,14]. We consider that defining a practitioner as 'expert' is especially difficult in CAM as training can vary widely (acupuncture training can range from 4 days to a degree course depending on the practitioners previous clinical background and acupuncture style taught). To avoid using misleading terminology, some Delphi papers avoid using the term 'expert' [6] and this was the approach we took (despite setting an inclusion criteria which should ensure some level of knowledge; participants were required to have completed a recognised training programme, be registered with a professional body and having at least three years clinical experience) We advise avoiding labelling participants but suggest being explicit about criteria used to include participants in a study. We also advise recognising the limitations of Delphi studies (identifying that results are 'group consensus' and not necessarily 'best', 'expert' or 'correct' results).

Another consideration when designing a Delphi study is the homogeneity or heterogeneity of the panel. It has been suggested that a diverse panel leads to better performance as it allows for a wider range of alternatives and perspectives [9] but depending on the study aim a homogenous group may be more appropriate in certain cases. Sample size is dependent on what is being investigated, the complexity of the problem, the homogeneity or heterogeneity of the sample and availability of resources [4]. In keeping with sample size recommendations for a homogenous sample (10–15 [10] or 8–12 participants [4]) many health related Delphi studies have a relatively small sample size, and recruit participants with particular knowledge of a condition [15,16,17]. In this study, as participants were relatively homogenous we aimed to recruit approximately 8-15 participants in each group. However, it could be argued that Delphi studies should have larger sample sizes to ensure generalizability and some studies have done this, recruiting large numbers of participants through random sampling [18]. Sample characteristics and size need to be carefully considered when designing a Delphi study.

4.2. Iteration

A common question in Delphi studies is how many rounds? The answer to this depends on whether consensus is being used as a 'stopping guideline' or if the number of rounds has been set *a priori*. Although the classic Delphi has four rounds [19] many studies set an *a priori* criterion of three rounds [7,20] but some only include two [21]. A limitation of including only two rounds is that stability cannot be confirmed [1]. As attrition is likely to increase with each round, to ensure against participant fatigue, but to ensure results are meaningful three rounds seems optimal. We included an *a priori* criterion of three rounds in our Delphi study, but also asked participants to rate the final protocol developed from the Delphi study. We suggest this may be a consideration for future studies.

4.3. Round 1

A Classical Delphi approach involves open-ended questions, generating qualitative data. Alternatively a modified approach can be taken with the researcher identifying issues through either a literature review, or consultation with stakeholders [4]. Studies using a classical approach ask varying numbers of questions (one open-ended question [7] 28 questions [21]). In our study, to develop a treatment protocol for a randomised controlled trial, we asked participants questions about 2 theoretical cases (12 questions about each case). However, despite taking a deductive stance and imposing an inclusion criterion for recirculation of statements, this produced a large number of statements meaning future rounds were lengthy and time consuming for participants. On reflection, we would recommend including fewer, well focused open-ended questions or using a modified approach to develop initial statements.

Some Delphi studies collect first round data in a 'real world' setting (interviews, focus groups) using an inductive form of analysis. If using this technique there should be awareness that during analysis it may be difficult to stay close to verbatim statements and although reducing raw responses into single statements goes against the logic of inductive analysis this may be

Table 2
Areas identified needing consideration with Delphi methodology.

1.	Paradigm under which the study is conducted (epistemological and ontological stance).
2.	Use of the term 'expert' when describing participants.
3.	Sample size and the heterogeneity or homogeneity of the sample.
4.	Iteration (number of rounds).
5.	Collection of round one data (classical or modified approach).
6.	Optimal number of responses categories of Likert scales in round two and subsequent rounds.
7.	Inclusion and exclusion of data in round three and subsequent rounds.
8.	Aggregation and participant feedback.
9.	Definition and conceptualisation of consensus.
10.	Distinguishing consensus, agreement and stability of response.
11.	Attrition.

necessary to allow for a manageable volume of subsequent data [22]. The difficulties of presenting qualitative data quantitatively should be carefully considered.

4.4. Round 2

Round two Delphi takes the form of a structured questionnaire, including statements generated from round one which are ranked on a Likert scale. However, few recommendations exist in the Delphi literature on the optimal number of response categories with different numbers being used, ranging from four points [8] to eleven point scales [17].

Establishing the reliability and validity of a scale is important. As little or no literature is currently available on the optimal number of response categories specifically in Delphi Likert scales, we have reviewed literature on studies evaluating optimal Likert scale response categories in non-specific types of questionnaires. Further research is needed to establish Delphi specific optimal number of response categories.

Non-Delphi specific studies have found that two, three and four point scales have poor reliability and discriminating power [23]. Although reliability and factorial validity has been shown to improve with increased number of responses [24] too many responses may lead to inconsistency in category interpretation and misleading results (categories with psychologically homogenous responses being arbitrarily divided [25]). Test-retest reliability has been reported to decrease for scales with more than 10 categories [23] and it has been suggested that the optimal number of categories lie between four to seven [24]. Additionally it has been found that participants favour scales of seven, nine and ten [23].

As well as considering the size of the Likert scale, researchers also need to decide whether to include a midpoint (odd number of categories) or not (even number of categories). An argument against including a midpoint is that it allows participants to remain neutral, which could be interpreted as "don't know", "undecided" and "no opinion" [26]. This could affect reliability and validity of results, if the midpoint is used as a "dumping ground" [27]. In our study we chose a six point scale as we wanted participants to have to make a positive or negative decision about each statement. Additionally we included a 'no comment' option for participants who did not feel qualified to rank a statement. This has also been done in other studies [20] and may be a consideration when designing a study if participants have varied qualifications and knowledge.

4.5. Gaining consensus

An important consideration when conducting a Delphi study is deciding what to include in subsequent rounds. Ideally all statements should be recirculated to ensure that data can be analysed fully. However, it has also been advocated that only statements which have not met consensus are recirculated in round three. This shortens the questionnaire and may reduce attrition, but also means that the recirculated questions have the chance of gaining a higher rating of importance than those which achieved consensus in round two [4]. Additionally, this approach means stability of response cannot be assessed across all statements as data is needed from both rounds [28,29]. In our study in round one each of the 12 questions generated a number of statements. In round three we compromised and excluded questions in which 50% or more of the ranked statements had met consensus. However, within questions included, ranked statements which had met consensus were not omitted to avoid introducing bias and the possibility of included statements gaining a higher rating of importance. Some studies include only statements which meet consensus in previous rounds [14]. However, although this means all statements included in the final round can be fully analysed, it also means statements which do not meet consensus are rejected without the opportunity for participants to reflect on their initial judgement. We advise careful thought of both round one data collection and analysis to avoid a lengthy second round which requires shortening in subsequent rounds.

Delphi studies require participants to receive feedback on results of previous rounds. Although there is no agreement on the best method of aggregation, to ensure participants have some indication of the extent of consensus, both central tendency and a measure of distribution should be included [1]. Medians tend to be preferred over means as they are more robust to the effect of outliers and IQR is considered more robust than standard deviation [1]. Some studies additionally provide visual feedback (bar charts) which can help with interpretation [7]. We did not provide bar charts in our study, but retrospectively acknowledge that providing information on the distribution of data would have been useful to participants.

4.6. Consensus

How consensus is defined in Delphi studies depends on the question being asked and the implication of the research [30]. Consensus can either be used to determine if agreement exists [20] or as a stopping guideline [28]. In our study we used consensus to determine if agreement existed and set an *a priori* criterion on number of rounds. Consensus has been conceptualised differently across Delphi studies and no agreement exist on which is the best criteria to use [28]. It has been determined through the aggregate of judgment, subjective level of central tendency and by confirming stability [20,28]. Consensus within rounds typically measures the agreement of the individual participant with the statement, which then provides group opinion and the extent to which participants agree with each other. Stability of response can indicate whether consensus was present throughout and whether it developed or changed between rounds [20]. A systematic review including 80 Delphi studies identified five main methods used to achieve consensus, the most frequently being median scores above a predefined threshold and a high level of agreement between panel members (for example, median score above a certain level and a certain percent of overall rating being in the lowest or highest tertile) [31]. Another systematic review of a random sample of 100 Delphi papers found that percent agreement was most frequently used [32].

Although it has been suggested that stability of response is the more reliable indicator of consensus [33] there is also the opinion that this measures internal reliability and not consensus [1]. It has been argued that reliability, agreement and consensus are different, with reliability measuring the proportional consistency of variance among raters [1] agreement measuring the extent to which participants agree with the statement under consideration and consensus measuring the extent to which participants agree with each other [30].

A study exploring different methods to measure consensus and stability in Delphi studies advised using a combination of statistics to reduce subjectivity and ensure validity of results [28]. Median and IQR are considered robust measures, with IQR accepted as an objective and rigorous way of determining consensus [34]. In our study we set different criteria for reliability, agreement and consensus. Consensus was determined through measurement of variance in response (IQR). We recommend being explicit about terminology and not confusing consensus with either stability/reliability or agreement.

4.7. Stability of response/internal reliability

Stability of response measures reliability of results and refers to the level of agreement between rounds. It is necessary to ensure

results are stable and reliable and it has been argued that consensus is meaningless if group stability has not been obtained [34]. The Chi-squared (X^2) has been used to test for stability, but there has been advice against using it in Delphi studies as it determines "the independence of the rounds from responses found in them" and not the stability of response between rounds [28]. Kappa statistics have been advocated with high or increasing kappa values demonstrating stability of individuals' views within the group [28]. However, Kappa is a measure for nominal scale agreement and assumes that rating has no natural ordering [34]. Tests which are suitable for use on ordinal data to test stability of response include the Wilcoxon matched-pairs signed rank test, which works with paired data of the same group of individuals in a before and after situation. Responses are considered stable when there is no significant change [34]. Stability of response could also be reported by providing data on the median and IQR across rounds [7,20] through graphical presentations of means and standard deviations [29] or with intraclass correlation coefficient (ICC) [1,35]. Providing data on the median and IQR across rounds provides data which is readily interpretable and we recommend this. We also recommend using the Wilcoxon matched-pairs signed rank test or ICC.

4.8. Attrition

Attrition can be a problem in Delphi studies and various techniques have been suggested to minimise this. These include; making participants feel like they are partners in the study, ensuring participants have an interest in the topic, ensuring participants take ownership (remind participants that each round is constructed on their previous responses), nurturing relationships [30]. Attrition may not have been a large problem in our study due to participant interest in the topic and because of the quick turnaround of data (deadline of 2 weeks for each round and each new round sent out two weeks after closure of the previous one). We recommend a short time frame as a means of maintaining participant interest.

5. Conclusion

Many papers describe the use of the Delphi technique. This paper has attempted to review areas which may need consideration and provide guidelines when designing a Delphi study. Using the term 'expert' to describe participants is problematic and has to be explicitly declared and clarified. To avoid participant fatigue and to ensure that data can be fully analysed an *a priori* criterion of three rounds is recommended. Round one data collection and analysis needs to be carefully considered to ensure a manageable amount of data is generated for subsequent rounds. Careful thought should be given to the number of categories of Likert scales and to the inclusion of a midpoint or not. Excluding data after round two ideally should be avoided. Graphical representation of results may benefit participants. The terms consensus, reliability and agreement should not be confused.

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Conflict of interest

None declared

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Appendix 4.3 Participant information sheet for Delphi study

Participant Information Sheet
Acupuncture in the Treatment of Phantom Limb Syndrome

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study? The aim of this study is to develop acupuncture guidelines / protocols for the management of phantom limb syndrome in lower limb amputees. The research is part of a MPhil / PhD degree at London South Bank University.

Approximately 5-6000 major limb amputations are carried out in the UK every year. One frequent complication post amputation is the risk of pain or altered sensation (known as phantom limb syndrome). Phantom limb syndrome has been reported to be prevalent in up to 80% of amputees and is difficult to treat with conventional medicine. Acupuncture has been shown to be effective in the treatment of chronic pain conditions but has not been widely assessed or documented in the treatment of phantom limb syndrome. Case studies which do record treating this condition with acupuncture use a wide variety of points and principles and there are no commonly recognised treatment regimes for this condition.

Why have I been chosen? You have been chosen to be invited to participate in this study if you:

- Have completed training in Acupuncture
- Are registered with either the British Acupuncture Council or the Association of Traditional Chinese Medicine or the Acupuncture Association of Chartered Physiotherapists
- Have at least 3 years clinical experience in acupuncture
- Are able to communicate orally and written in English
- It is NOT necessary to have treated any patients with phantom limb syndrome

What is involved? It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep. If you email us back we assume this means you consent to participate in the study. You are still free to withdraw anytime up to the submission of the study and without giving a reason.

If you are willing to participate, you will be:

- invited to complete 2-4 questionnaires which will be sent to you electronically. It is anticipated that you will have to complete only 3 questionnaires but

depending on peoples answerers it may only be 2 or could be as many as 4 questionnaires.

- The first questionnaire will take no more than 20 minutes to complete and will explore your views from a Traditional Chinese Medicine perspective on the pathology and treatment of phantom limb syndrome. Subsequent questionnaires should be much quicker to complete (approximately 10-15 minutes) and will involve you tick box rating your views on the pathology and treatment of phantom limb syndrome.
- There are no right or wrong answers to the questions. The study is seeking your opinion.

You will be asked to complete each questionnaire within 7 days of circulation and each subsequent questionnaire will be sent to you at 3-4 week intervals. The study is planned to last up to 3-4 months in total.

It is not anticipated that you will be at any disadvantage or suffer any risk from participating in this study.

It is unlikely that you will gain any personal benefit from participating in this research. However, the information you share with the researcher will contribute to understanding views on the Traditional Chinese Medicine pathology of phantom limb syndrome. Your views will also contribute to clinical acupuncture practice and research by contributing to help devise acupuncture protocols for the treatment of this condition.

You are free to withdraw from the study and not have your information included, at any time up to the time of completion of the study. However, once the thesis is submitted for examination data cannot be withdrawn.

Is it confidential? All information received from you will be handled in a confidential manner and stored in a locked filing cabinet and on a password protected computer in an environment locked when not occupied. Only the researcher and supervisor will have direct access to the information. Any reference to you will be coded. This information will be held for 5 years post award of a doctorate. .

Who is organising the research? This study is being completed as part of a MPhil / PhD degree at London South Bank University. It has been reviewed and ethically approved by the London South Bank University Research Ethics Committee.

Further information: If you have a concern about any aspect of this study, you should ask to speak with the researcher who will do their best to answer your questions (Esme Trevelyan: tel: 07768 348407 email: trevelye@lsbu.ac.uk). If you wish any further information regarding this study or have any complaints about the way you have been dealt with during the study or other concerns you can contact the director of studies: Prof Nicola Robinson at LSBU tel: 0207 815 7940, who is the Academic Supervisor for this study. Finally, if you remain unhappy and wish to complain formally, you can contact the Chair of the University Research Ethics Committee (email ethics@lsbu.ac.uk). Details can be obtained from the university website: https://my.lsbu.ac.uk/page/research-degrees-ethics

Appendix 4.4 Round 1 Delphi questionnaire

Acupuncture for the Treatment of Phantom Limb Pain / Sensation

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Thank you for taking the time to complete this survey.
The aim of the survey is to guide the use of acupuncture for phantom limb syndrome.
It does not matter if you have never treated phantom limb syndrome.
It is expected the questionnaire will take no longer than 20 minutes to complete.
If you could return the questionnaire within two weeks we would be most grateful. If you need to discuss any aspect of this further please contact Esme Trevelyan (email trevelye@lsbu.ac.uk / tel: 07768 348407).
Thank you for agreeing to participate in this study.

Instructions

The survey consists of three sections. Section one requests information about yourself and your acupuncture practice. Section two and three are hypothetical case studies about amputees with phantom limb syndrome.
We would like to know how you would treat phantom limb syndrome as a practitioner (even if you have not had past experience in treating this condition).
Return of the questionnaire implies consent to participate.

Continue >

Acupuncture for the Treatment of Phantom Limb Pain / Sensation

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Information about yourself

Personal details

Please complete all questions

1. What is your study ID number?

2. What is your gender?

○ Male ○ Female

3. What is your age?

○ 21-30 ○ 31-40 ○ 41-50 ○ 51 or above

4. What is your background?
(select all that apply)

- [ ] Acupuncturist (e.g. TCM, 5 element, Chinese, Japanese acupuncturist)
- [ ] Western Medical Acupuncturist
- [ ] Physiotherapist practicing acupuncture
- [ ] Other **(please specify)**:

5. Are you a member of a professional association?
(select all that apply)

- [ ] British Acupuncture Council
- [ ] Association of Traditional Chinese Medicine
- [ ] Chartered Society of Physiotherapy
- [ ] Not a member of a professional association
- [ ] Other **(please specify)**:

Details about your acupuncture practice

6. Where did you study acupuncture?
(select all that apply)

- [ ] UK
- [ ] China
- [ ] Other **(please specify)**:

7. What style of acupuncture do you practice
(select all that apply)

- [ ] TCM Acupuncture
- [ ] 5 Element Acupuncture
- [ ] Western Medical Acupuncture
- [ ] Other **(please specify)**:

8. How many years have you been in practice as an acupuncturist?

- ○ 0-5 years ○ 6-10 years ○ 11-20 years ○ 21+ years

9. Do you practice

- ○ Full time ○ Part time ○ Not currently in practice

10. Do you have an area of speciality for example fertility acupuncture, cosmetic acupuncture, musculoskeletal acupuncture?

- ○ No ○ Yes (if giving details please tick other)
- ○ Other **(please specify)**:

11. Have you ever treated a patient for phantom limb syndrome?

- ○ Yes ○ No

12. If you have treated amputees for phantom limb syndrome, approximately how many have you treated? **(Optional)**

Continue >

Acupuncture for the Treatment of Phantom Limb Pain / Sensation

CASE STUDY 1

Below is a case study of an amputee suffering from phantom limb syndrome. Please read the information provided and answer the following questions. If you are a western / medical acupuncturist please write not applicable to any questions which are not applicable to your training.

A 75 year old male with a 20 year history of type II diabetes had been suffering long term diabetic neuropathy and peripheral arterial disease (atherosclerosis). He developed an ulcer in his left toe due to the neuropathy and peripheral arterial disease which eventually led to him having a left transtibial amputation (amputation through the lower limb but maintaining the knee joint) 15 days ago. Prior to surgery he suffered from numbness and pain for over a year in both lower limbs and especially the soles of the feet due to the diabetic neuropathy (sharp stabbing, shooting sensations and a loss of sensation) and his ankles and feet were swollen and cold to touch. Symptoms were aggravated by cold weather and eased with warmth.

Post amputation the patient complained of phantom limb pain and stump pain in his left lower limb. Pain was described as heaviness in the stump and a feeling that the missing limb was constantly twisted and contracted. Constant pins and needles and intermittent sharp electric shock like sensations were felt in the missing limb especially the foot. Phantom limb pain was rated 8/10 in intensity and was constantly present.

History of present disease: Type 2 diabetes, poorly controlled blood sugar (sometimes high / sometimes low), loose stools, normal appetite, normal sleep and regular urination, dark pale tongue with white coating, deep thready pulse.

Diagnosis and Treatment

13. What pathology / syndromes would you diagnose this patient with (for example liver qi stagnation etc.)? **(Optional)**

14. What would be you main treatment principles when treating this patient?

15. Would you use body, auricular or scalp acupuncture or a combination of any of these in the treatment of this patient?
(select all that apply)

- ☐ body acupuncture
- ☐ auricular acupuncture
- ☐ scalp acupuncture

16. If using body acupuncture which limb(s) would you needle?

- opposite limb to amputation
- the remaining limb / stump
- neither lower limbs
- both lower limbs

17. What specific points would you use to treat the underlying pathology causing phantom limb pain in this case study and why (please include body, scalp, auricular points as you feel appropriate)? Please also state whether you would needle bilaterally or unilaterally and describe the needle technique for each point (tonify / even / sedate).

18. Would you try to obtain deqi when treating this patient?

- Yes
- No
- Unsure

19. How long would you retain the needles for?

- No retention
- 10 minutes
- 20 minutes
- 30 minutes
- 40 minutes or more

20. Would you manipulate the needles during treatment and if so how frequently?

Adjunctive treatment and number of treatments

21. Would you use electro-acupuncture (EA)?

- Yes
- No
- Unsure

22. Would you use cupping or moxa or any other adjunctive treatment on this patient?

23. How often / frequently would you treat this patient?

24. How many treatments would you anticipate giving in total for a course of treatment?

Thank you for completing case study 1.

The next page will ask you the same questions about case study 2.

Continue >

Acupuncture for the Treatment of Phantom Limb Pain / Sensation

CASE STUDY 2

A healthy 40 year old male had been involved in a road traffic accident 2 weeks ago which resulted in a right hip disarticulation, (amputation through the hip joint, removing the entire leg). Prior to amputation the patient was in good general health. He had suffered occasional low back pain (due to prolonged sitting at a desk at work) but was otherwise well.
Post amputation the patient complained of constant stabbing and shooting pain in his missing limb (7/10 intensity) especially deep in the thigh where it was injured in the road traffic accident.
The patient also complained of poor sleep, stress and emotional upset, poor appetite and slight constipation. Tongue was purple / dark with a red tip and pulse was choppy.

Diagnosis and Treatment

25. What pathology / syndromes would you diagnose this patient with (for example liver qi stagnation etc.)? **(Optional)**

26. What would be you main treatment principles when treating this patient?

27. Would you use body, auricular or scalp acupuncture or a combination of any of these in the treatment of this patient? If a combination what combination? (e.g. auricular and body)
(select all that apply)

- ☐ body acupuncture
- ☐ auricular acupuncture
- ☐ scalp acupuncture

28. If using body acupuncture which limb(s) would you needle?

- opposite limb to amputation
- the remaining limb / stump
- neither lower limbs
- both lower limbs

29. What specific points would you use to treat the underlying pathology causing phantom limb pain in this case study and why (please include body, scalp, auricular points as you feel appropriate)? Please also state whether you would needle bilaterally or unilaterally and describe the needle technique for each point (tonify / even / sedate).

30. Would you try to obtain deqi when treating this patient?

- Yes
- No
- Unsure

31. How long would you retain the needles for?

- No retention
- 10 minutes
- 20 minutes
- 30 minutes
- 40 minutes or more

32. Would you manipulate the needles during treatment and if so how frequently?

Adjunctive treatment and number of treatments

33. Would you use electro-acupuncture (EA)?

- Yes
- No
- Unsure

34. Would you use cupping or moxa or any other adjunctive treatment on this patient?

35. How often / frequently would you treat this patient?

36. How many treatments would you anticipate giving in total for a course of treatment?

Thank you for completing case study 2

Continue >

Acupuncture for the Treatment of Phantom Limb Pain / Sensation

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Thank you

Many thanks for taking the time to complete this survey. It is very much appreciated.
The survey has been approved by London South Bank University Research Ethics Committee
We will let you know the results as soon as possible.
THANK YOU

Esme

Appendix 4.5 Ethical approval letter from London South Bank University for the Delphi study

London South Bank University

Direct line: 020-7815 6025 E-mail: mitchen5@lsbu.ac.uk
Ref: UREC 1327

Esme Trevelyan
201 Blazer Court
28A St Johns Wood Road
London
NW8 7JY

Dear Esme,

Re: Acupuncture in the treatment of phantom limb syndrome I wish to commence data collection in September 2013

Thank you for submitting this proposal and for your response to the reviewers' comments.
I am pleased to inform you that Full Chair's Approval has been given by Chair on behalf of the University Research Ethics Committee.
I wish you every success with your research.

Yours sincerely,

N Mitchell

Nicola Mitchell
Secretary, LSBU Research Ethics Committee

cc:
Prof Shushma Patel, Chair, LSBU Research Ethics Committee

Appendix 4.6 List of statements which met consensus and agreement

List of Statements which met consensus and agreement, not treated phantom limb pain (NTPLSd) group, case study 1

Statement	Round	Median (quartiles)	IQR	Range	No comment	P value
Qu 1. What pathology / syndromes would you diagnose this patient with?						
Spleen qi deficiency	2	5 (5-6)	1	2	5	
Blood deficiency	2	5 (4-5)	1	2	5	
Damp in / obstructing the channels	2	5 (4.25-5.75)	1.5	2	4	
Qu 2. What would be your main treatment principle when treating this patient?						
Decrease and relieve pain	2	5.5 (5-6)	1	2	0	
Move qi and blood and clear stagnation	2	5 (5-5.75)	0.75	3	4	
Tonify spleen (qi / yang)	2	5 (5-6)	1	2	5	
Clear damp and phlegm	2	5 (5-6)	1	2	5	
Nourish / tonify blood	2	5 (4-5)	1	4	4	
Qu 3. Would you use body, auricular or scalp acupuncture or a combination of any of these in the treatment of this patient?						
Body and auricular acupuncture only	2 3	5 (4-6) 5 (4-6)	2 2*	4 4	1 2	0.71
Qu 4. If using body acupuncture which limbs would you needle?						
Both lower limbs	2 3	5 (5-5.75) 5 (4-6)	0.75 2**	4 5	0 0	0.49
Qu 5a. What specific points would you use to treat the underlying pathology causing PLP in this case study and why (auricular)?						
Shenmen	2 3	5.5 (4-6) 5.5 (5-6)	2 1	2 2	4 4	0.56
Sympathetic	2 3	5 (4-6) 5 (4.5-6)	2 1.5	2 2	5 3	1
Points relating to the lower limb	2 3	6 (5-6) 5 (4-6)	1 2**	1 3	3 3	0.1
Qu 5b. What specific points would you use to treat the underlying pathology causing PLP in this case study and why (body)?						
LR3 (liver 3)	2	5 (5-5)	0	4	1	
Local points on stump depending on healing (health of local tissue) and patient's reaction	2	5 (5-5.75)	0.75	4	0	
GV20 (governor vessel 20)	2	5 (4-5)	1	4	1	
SP6 (spleen 6)	2	5 (4-5)	1	3	2	

SP3 (spleen 3)	2	5 (4-5)	1	2	3	
Points on the lower back taking a segmental approach to dermatomal pain	2	5 (4-5.5)	1.5	3	3	
SP9 (spleen 9)	2	5 (4-5.5)	1.5	2	3	
SP10 (spleen 10)	2	5 (4.5-6)	1.5	2	3	
4 Gates (LI4 + LR3)	2	5 (4.25-6)	1.75	4	0	
Qu 6. Would you try and obtain deqi when needling this patient?						
Yes - will try and obtain deqi	2	5 (4.25-6)	1.75	3	0	
Qu. 7 How long would you retain the needles for?						
20-30 minutes	2	5 (4.25-6)	1.75	4	0	
Qu 8. Would you manipulate the needles during treatment and if so how frequently?						
Once or twice	2 3	4 (2-5) 4***(3-4)	3 1	5 5	1 1	0.32
Qu 9. Would you use electro acupuncture?						
Consensus not met						
Qu 10. Would you use cupping, moxa or any other adjunctive treatment?						
Consensus not met						
Qu 11. How often / frequently would you treat this patient						
Weekly	2	5 (4-5)	1	5	1	
Reduce frequency as symptoms abate	2	5 (5-6)	1	5	0	
Qu 12. How many treatments would you anticipate giving in total for a course of treatment?						
At least six	2	5.5 (4.25-6)	1.75	4	0	

Key: *consensus not met but statement included as IQR ≤ 2; **consensus not met in this round but statement met consensus and agreement in round 2; ***agreement not met but statement included as statement score 4 (somewhat agree).

List of Statements which met consensus and agreement, treated phantom limb pain (TPLSd) group, case study 1

Statement	Round	Median (quartiles)	IQR	Range	No comment	P value
Qu 1. What pathology / syndromes would you diagnose this patient with?						
Qi and blood stagnation	2	6 (5-6)	1	2	0	
Spleen qi / yang deficiency	2	5 (5-6)	1	3	0	
Kidney deficiency	2	5 (4.5-6)	1.5	2	2	

Qu 2. What would be your main treatment principle when treating this patient?						
Reduce pain	2	6 (6-6)	0	0	0	
Move qi and blood	2	5 (5-6)	1	2	0	
Qu 3. Would you use body, auricular or scalp acupuncture or a combination of any of these in the treatment of this patient?						
Auricular and body acupuncture	2	6 (6-6)	0	0	1	
Qu 4. If using body acupuncture which limbs would you needle?						
Opposite limb to amputation	2	6 (4.75-8)	1.25	2	1	
Qu 5a. What specific points would you use to treat the underlying pathology causing PLP in this case study and why (auricular)?						
Points corresponding to the lower limb	2	6 (5.25-6)	0.75	3	1	
Shenmen	2	6 (4.75-6)	1.25	2	1	
Qu 5b. What specific points would you use to treat the underlying pathology causing PLP in this case study and why (body)?						
Mirroring local points around stump by needling them on the opposite limb	2 3	5 (4.5-6) 5 (4-5)	1.5 1	3 2	1 0	0.71
Qu 6. Would you try and obtain deqi when needling this patient?						
Yes try to obtain deqi	2	6 (5-6)	1	1	0	
Qu. 7 How long would you retain the needles for?						
30 minutes	2 3	4 (3-6) 5 (3-5)	3 2*	4 2	0 0	0.41
Qu 8. Would you manipulate the needles during treatment and if so how frequently?						
Consensus and agreement not met						
Qu 9. Would you use electro acupuncture?						
Consensus and agreement not met						
Qu 10. Would you use cupping, moxa or any other adjunctive treatment?						
Consensus not met						
Qu 11. How often / frequently would you treat this patient?						
2 times weekly	2	5 (4-5)	1	4	0	
Qu 12. How many treatments would you anticipate giving in total for a course of treatment?						
About 10 treatments	2	5 (4-5)	1	3	0	

Key: *= consensus not met but statement included as IQR ≤ 2

List of Statements which met consensus and agreement, not treated phantom limb pain (NTPLSd) group, case study 2

Statement	Round	Median (quartiles)	IQR	Range	No comment	P value
Qu 1. What pathology / syndromes would you diagnose this patient with?						
Shen disturbed	2	5 (5-5)	0	2	3	
Qi and blood stagnation	2	5 (5-6)	1	2	5	
Blood stagnation	2	5 (5-6)	1	1	6	
Spleen qi deficiency	2	5 (4-5)	1	1	5	
Qu 2. What would be your main treatment principle when treating this patient?						
Reduce pain	2	6 (5-6)	1	3	0	
Move qi and blood	2	6 (5-6)	1	1	5	
Harmonise liver qi	2	5 (4-5)	1	1	5	
Tonify spleen	2	5 (4-5)	1	1	5	
Nourish the heart	2	5 (4-5)	1	2	5	
Reduce stress and calm the mind	2	5 (5-6)	1	4	1	
Qu 3. Would you use body, auricular or scalp acupuncture or a combination of any of these in the treatment of this patient?						
Body acupuncture	2 3	5 (4-6) 5 (4-6)	2 2*	5 5	1 0	0.53
Qu 4. If using body acupuncture which limbs would you needle?						
Opposite limb to amputation	2 3	5 (3.25-6) 5.5 (4-6)	2.75 2*	3 5	0 0	0.75
Qu 5a. What specific points would you use to treat the underlying pathology causing PLP in this case study and why (auricular)?						
Shenmen to calm the mind and reduce stress	2	6 (5-6)	1	3	1	
Qu 5b. What specific points would you use to treat the underlying pathology causing PLP in this case study and why (body)?						
4 Gates (for pain relief)	2 3	6 (5-6) 6 (5-6)	1 1	2 3	0 0	0.56
Bladder points at lumbar level	2 3	5 (4-6) 5 (4.25-6)	2 1.75	3 2	1 0	0.26
Segmental points around lumbar 1 and 2 as they innervate the hip joint	2 3	5 (4-5) 5 (4-5.75)	1 1.75	5 5	1 0	0.32

LR3 (liver 3) even	2 3	5 (4-5.25) 5 (5-5)	1.25 0	2 2	2 0	0.41
GB34 (gall bladder 34)	2 3	5 (4-5.25) 5 (5-5)	1.25 0	2 2	2 1	0.79
Internal dragons (CV15, ST25, ST32, ST41)	2 3	5 (4-6) 5 (4-5)	2 1	2 3	6 5	0.18
SP10 (spleen 10) (to move blood)	2 3	5 (4-6) 5 (4-5)	2 1	2 2	1 1	0.03[P]
ST36 (stomach 36)	2 3	5 (4-5) 5 (4-5)	1 1	3 2	1 1	1
GV20 (governor vessel 20)	2 3	5 (4-6) 5 (4-5)	2 1	3 3	1 0	0.92
HT7 (heart 7)	2 3	5 (5-6) 5 (4-5)	1 1	2 2	1 1	0.23
PC6 (pericardium 6)	2 3	5 (4-6) 5 (4-5)	2 1	3 3	1 1	1
Qu 6. Would you try and obtain deqi when needling this patient?						
Yes - will try and obtain deqi	2	5 (5-6)	1	2	0	
Qu. 7 How long would you retain the needles for?						
20-30 minutes	2 3	5 (4-6) 6 (5-6)	2 1	3 1	0 0	0.04[P]
Qu 8. Would you manipulate the needles during treatment and if so how frequently?						
Consensus and agreement not met						
Qu 9. Would you use electro acupuncture?						
Consensus and agreement not met						
Qu 10. Would you use cupping, moxa or any other adjunctive treatment?						
Consensus and agreement not met						
Qu 11. How often / frequently would you treat this patient?						
Space out treatments as patient improves	2	5.5 (5-6)	1	2	0	
Weekly	2	5 (4-5)	1	4	1	
Twice weekly	2	5 (4-5.75)	1.75	3	0	
Qu 12. How many treatments would you anticipate giving in total for a course of treatment?						
Approximately 10	2	5 (4-5)	1	3	0	

Key: *consensus not met but statement included as IQR ≤ 2; [P]p <0.05

List of Statements which met consensus and agreement, treated phantom limb pain (TPLSd) group, case study 2

Statement	Round	Median (quartiles)	IQR	Range	No comment	P value
Qu 1. What pathology / syndromes would you diagnose this patient with?						
Qi and blood stagnation	2	6 (5-6)	1	1	1	
Liver qi stagnation	2	5 (5-6)	1	2	0	
Qu 2. What would be your main treatment principle when treating this patient?						
Manage and reduce pain	2	6 (6-6)	0	0	0	
Move qi and blood	2	6 (5-6)	1	1	0	
Calm the mind	2	6 (5-6)	1	2	0	
Move liver qi	2	5 (5-6)	1	1	0	
Qu 3. Would you use body, auricular or scalp acupuncture or a combination of any of these in the treatment of this patient?						
Body and auricular acupuncture	2	6 (6-6)	0	0	1	
Qu 4. If using body acupuncture which limbs would you needle?						
Opposite limb to amputation	2	5 (5-6)	1	1	0	
Qu 5a. What specific points would you use to treat the underlying pathology causing PLP in this case study and why (auricular)?						
Shenmen (to manage stress and anxiety)	2	6 (5.5-6)	0.5	2	1	
Sympathetic (to manage stress and anxiety)	2	6 (4.75-6)	1.25	2	1	
Points for the lower limb	2	6 (4.5-6)	1.5	3	1	
Qu 5b. What specific points would you use to treat the underlying pathology causing PLP in this case study and why (body)?						
LR3 (liver 3)	2 3	6 (5-6) 5 (5-6)	1 1	1 2	0 0	0.08
GB34 (gall bladder 34)	2 3	6 (5-6) 5 (5-6)	1 1	1 2	1 0	0.08
Bladder points in lumbar and sacral area	2 3	5 (4-6) 5 (5-6)	2 1	2 2	0 0	1

Yintang	2 3	5 (5-6) 5 (5-5)	1 0	1 2	1 0	0.32
Distal points on opposite limb mirroring phantom pain	2 3	5 (5-6) 5 (4-5)	1 1	1 2	0 0	0.16
PC6 (pericardium 6) regulates heart, calm spirit, harmonises stomach	2 3	5 (4.5-6) 5 (4-5)	1.5 1	2 1	2 0	0.08
Qu 6. Would you try and obtain deqi when needling this patient?						
Yes try and obtain deqi	2	6 (5-6)	1	1	0	
Qu. 7 How long would you retain the needles for?						
20-30 minutes	2	6 (5-6)	1	1	0	
Qu 8. Would you manipulate the needles during treatment and if so how frequently?						
Manipulate needles 2-3 times depending on patient sensitivity	2	5 (4.25-5)	0.75	3	1	
Qu 9. Would you use electro acupuncture?						
Consensus not met						
Qu 10. Would you use cupping, moxa or any other adjunctive treatment?						
Consensus and agreement not met						
Qu 11. How often / frequently would you treat this patient?						
2 times a week	2 3	5 (3-6) 5 (5-5)	3 0	5 4	0 0	0.74
Qu 12. How many treatments would you anticipate giving in total for a course of treatment?						
6-8 treatments	2	5 (4-5)	1	3	0	

Appendix 5.1 Published paper on the perceptions of phantom limb pain in lower limb amputees

Original Article

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Perceptions of phantom limb pain in lower limb amputees and its effect on quality of life: a qualitative study

Esmé G Trevelyan, Warren A Turner and Nicola Robinson

Abstract

Background: Phantom limb pain (PLP) is a prevalent complication post-amputation. Currently, qualitative literature exploring the experience of PLP in amputees is sparse, and little is known about whether the educational needs of amputees are being met.

Objectives: To explore lower limb amputees' descriptive lived experiences of PLP, to understand how PLP affects quality of life and to determine whether amputees feel they are provided with adequate information about PLP.

Methods: A qualitative descriptive approach, situated under the constructivist paradigm was taken, consisting of cross-sectional semi-structured interviews. A purposive sample of 15 lower limb amputees, 1–3 months post-surgery with past or current experience of PLP were interviewed once about their experience of PLP. Interviews were audio-recorded, transcribed verbatim and analysed using Framework Analysis. Interviews were conducted while participants were inpatients at an amputee rehabilitation unit in London.

Results: Six key themes were identified during analysis, of which three were related to PLP and are reported on in this article (real and physical phantoms, living with a phantom and being informed). PLP had numerous painful qualities. The phantom felt real, with kinetic and kinaesthetic properties. PLP had multiple meanings to amputees, was considered a reminder of circumstances and could affect quality of life. Information provided about PLP was inadequate.

Conclusion: PLP can be a severe and annoying experience acting as a reminder of amputees' circumstances. Information provided about PLP is inadequate, with some amputees still perceiving PLP as mental and imaginary. Education about PLP and awareness and accessibility to non-pharmacological interventions needs to be improved.

Keywords

Qualitative research, phantom limb, interview, education, communication

Introduction

Each year, approximately 5–6000 people undergo major limb amputation in England.[1] Phantom limb pain (PLP) and phantom limb sensations (PLS) are common complications post-amputation, and prevalence of PLP has been reported to be as high as 75–80%.[2,3] PLP is a chronic condition which may be present for many years.[4] It usually occurs within the first week of amputation, but can also occur years later.[5] Although generally it is assumed that PLP decreases slightly over time,[6] this is not always true.[7] No association between age, gender, cause of limb loss of marital status has been identified.[7] No difference has been found between prevalence of PLP in two very

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Table 1. Qualitative studies identified in a systematic review describing the experience of phantom limb syndrome.

Author	Date	Title	Journal
Shukla GD, Sahu SC, Tripathi RP, Gupta DK.	1982	Phantom limb: a phenomenological study.	*The British Journal of Psychiatry*
Mortimer C, Steedman WM, McMillan IR, Ravey J.	1998	Phantom pain II: patients' experiences, beliefs and knowledge.	*British Journal of Therapy and Rehabilitation*
Mortimer CM, Steedman WM, McMillan IR, Martin DJ, Ravey J.	2002	Patient information on phantom limb pain: a focus group study of patient experiences, perceptions and opinions.	*Health and Education Research*
Bosmans JC, Suurmeijer TPBM, Hulsink M, van der Schans CP, Geertzen JHB, Dijkstra PU.	2007	Amputation, phantom pain and subjective well-being: a qualitative study.	*International Journal of Rehabilitation Research*
Björkman B, Arner S, Lund I, Hyden LC.	2010	Adult limb and breast amputees' experience and descriptions of phantom phenomena – a qualitative study.	*Scandinavian Journal of Pain*
Björkman B, Arner S, Lund I, Hyden LC.	2012	Phantom phenomena – their perceived qualities and consequences from the patient's perspective.	*Scandinavian Journal of Pain*
Evans CB.	2014	Content analyses of a priori qualitative phantom limb pain descriptions and emerging categories in mid-southerners with limb loss.	*Rehabilitation Nursing*

different demographic groups.[4] However, a longitudinal study found the chance of suffering PLP was reduced in men and in lower limb amputees compared to women and upper limb amputees.[6]

Pain mechanisms involved in PLP include formation of neuroma and ectopic discharge. Peripheral noxious stimuli cause central sensitisation (increased spontaneous activity of dorsal horn neurons, increased responsiveness to afferent input, after discharge, expansion of receptive fields, wind-up a reduction in inhibitory processes and structural changes at the central nerve endings[8]). Cortically, there is reorganisation of areas including the somatosensory and motor cortex. Cortical fields which are deprived of input shrink, and receptive fields become smaller.[9]

Quantitative studies do not explore amputees' lived experience of PLP, and few qualitative studies exist (a systematic literature search of PubMed, AMED, CINAHL, MEDLINE, PsycINFO and ScienceDirect identified only seven studies (Table 1)). These studies report a range of experiences, attitudes and emotions associated with PLP but often do not report specifically on upper or lower limb amputation. Also, time since amputation often varies widely, and studies do not report on the effect of PLP on quality of life. No recent UK studies have explored whether information provided to amputees about PLP is adequate.

The aim of this study was developed through review of the literature and was to explore lower limb amputees' descriptive experiences of PLP, to understand how PLP affects quality of life and to determine whether amputees feel they are provided with adequate information about PLP. The study was nested in a larger study evaluating the feasibility of providing acupuncture for PLP.

Methods

The study was undertaken at the inpatient Amputee Rehabilitation Unit (ARU), Guy's and St Thomas' National Health Service (NHS) Foundation Trust, London, between December 2013 and June 2014. Ethical approval was granted by National Research Ethics Service (NRES) Committee London – Brent and London South Bank University. This cross-sectional study employed a qualitative descriptive design situated under the constructivist paradigm and consisted of face-to-face semi-structured interviews.

In order to ensure some variation, purposive sampling was used and 15 participants recruited (the planned purposive sample quota is presented in Table 2). This number was deemed adequate taking into consideration the purpose of the research, the objective of the analysis and the time and resources available. Data saturation was anticipated to occur within this number of interviews. Potential participants were identified by ARU physiotherapists, approached by the researcher (who had no prior contact with the participants) and provided with verbal and written information about the study. All participants were advised to take a minimum of 24 hours before consenting to participate.

Inclusion criteria included male or female, 18 years or above, lower limb amputation (greater than a toe),

Table 2. Purposive sample quota for selection of participants.

Sample quota			
	Vascular amputation	Trauma/disease/infection causing eventual amputation	Trauma/disease/infection causing immediate amputation
Males			
⩽65 years	1–4	1–3	1–2
>65 years	1–4	1–3	
Females			
⩽65 years	1–4	1–3	0–2
>65 years	1–4	1–3	

current or past experience of PLP, full cognitive ability (as assessed by the medical team) and ability to communicate in English. Exclusion criteria were severe other health complications.

All participants were interviewed once in a room where only the researcher (E.G.T.) and participant were present. Interviews were semi-structured, followed a topic guide (Figure 1), were audio-recorded and lasted approximately 1 hour. Interviews were structured to commence with demographic details, followed by a history of the events leading up to amputation and experience of PLP. The interview finished with discussion of the possibility of having acupuncture as an intervention and completing and providing feedback on outcome measures. Field notes were taken.

Data analysis

As E.G.T. had prior knowledge of PLP and had carried out a systematic review on the lived experience of PLP, a completely naive stance was not taken, but overall, the study was considered inductive due to the nature of the interviews, the predominately open coding and the allowance for emergence of new categories. Framework analysis, developed by Ritchie and Spencer, was used to analyse data. Within 24 hours of the interview, E.G.T. listened to audio-recordings, completed field notes and transcribed interviews verbatim. The steps of framework analysis were followed:

1. *Familiarisation*. E.G.T. became familiar with the data.
2. *Coding*. A combination of open and predefined codes were used.
3. *Identifying an analytic framework*. Drawing on both a priori data (such as the interview topic guide) and emergent issues, categories were developed both inductively from the data and deductively.
4. *Indexing*. The analytic framework was applied systematically to all data.
5. *Charting*. Was thematic and clearly referenced.
6. *Descriptive analysis*. Data were classified under higher order labels.
7. *Mapping/interpretation*. Key characteristics of the data were identified.

NVivo 10 was used to develop the analytic framework and index transcripts. Excel was used during charting and descriptive analysis. To ensure credibility, respondent validation was obtained post transcription of interviews (transcripts were returned to participants for approval) and peer debriefing took place throughout the research process (N.R. and W.T.). To ensure dependability, two researchers (N.R. and E.G.T.) separately coded three transcripts and the results were compared. Also, two researchers (N.R. and E.G.T.) independently coded and indexed a transcript using the analytic framework.

The researcher

The researcher (E.G.T.) was a chartered physiotherapist and acupuncturist with no relationship with participants prior to commencement of the study. Participants were unaware of her background.

Results

A total of 17 lower limb amputees were approached, of which 16 agreed to participate. One dropped out after interview, and one interview was terminated early (due to participant fatigue). Demographics of participants included in the study are shown in Table 3. Throughout the duration of the study, no women ⩽65 years were identified who had undergone amputation due to vascular pathology. Therefore, the original planned purposive quota was not fully achieved. Six key themes were identified during analysis, presented in Figure 2. This article reports only on the themes related to PLP.

Main questions

- Could you tell me about the events leading up to your amputation?
- Can you tell me about any pain you experienced prior to amputation in your amputated leg?
- Can you tell me about any experience of pain / sensations you have experienced since your amputation in your amputated leg (phantom pain)?
- How does the phantom pain / sensations affect you in your day to day life?
- What information were you given from anyone about phantom pain / sensations?
- Can you tell me about any past experience you have had of acupuncture?
- How would you feel about receiving acupuncture for the pain in your missing leg?

Figure 1. Summary of the interview topic guide.

Table 3. Participant demographic information.

P ID	Age	Gender	Ethnicity	Amputation level	Time since amputation	Reason for amputation	Previous amputations
1	54	M	White British	BK	2m	V/U	No
2	58	M	Black British	AK	2m	V	No
3	84	F	White British	BK	2m	V/U	No
6	75	M	White British	AK	3m	V	No
7	26	M	White British	BK	1m	T	No
8	62	M	White British	AK	1m	T/I	No
9	66	M	White Irish	AK	1m	V	No
10	60	M	White British	AK	1m	T/I	No
11	67	M	White British	TK	1m	V/U	No
12	35	M	White Other	BK	3m	T	No
13	54	F	White British	AK	1m	T/I	No
14	66	M	Mixed Caribbean	BK	1m	T/I	No
15	45	M	White British	BK	1m	V/U	No
16	82	F	White British	BK	1m	T/I	No
17	35	M	White British	BK	1m	V/U	Yes (toes and part of foot)

P: participant; M: male; F: female; BK: below knee; AK: above knee; TK: through knee; m: months; V: vascular; U: ulcer; T: trauma; I: infection.

Real and physical phantoms

This theme describes the physicality and the realness of the phantom. PLP was usually experienced distally, location could be described precisely and PLP was perceived as real and physical (as if it still belonged to the intact body). Numerous descriptions, usually metaphorical, were used to describe quality and revealed suffering. The most frequently described quality was the feeling of the phantom being tightly bound/being in a vice. Most participants described a whole variety of qualities of pain and non-painful sensations. PLP was usually described as constant and intensity varied from mild to excruciating pain:

> I feel as though, at the moment the sensation I get is I feel as though my foot is tightly bandaged and I can't do much about it … it's odd it's as though I want to undo the bandages and make the feeling go away. (P16)

> I did say once if I had a, I know its stupid thing to say, but if I had an axe I would chop the foot off. That's how bad it is. But of course I haven't got a foot to chop off! (P13)

Many participants felt PLP had improved since onset (but was not necessarily still improving). Six participants reported changes in quality and location of pain, including feeling an increased variety of sensations, PLP moving distally/proximally and covering a larger area.

Participants generally had a very real perception of the missing limb. A total of 14 participants described feeling the limb was still present, and some forgot their limb had been amputated. One had fallen because of this:

> I've got toe nails as well, you know, on this one … I feel as if I've got a shin there, and toenails and an ankle. (P3)

> and I'll go to automatically move my leg and then I'll think you silly sod it's not there! (P1)

Participants tried using the phantom, for example, to itch/scratch and take a shoe off the residual limb. Phantoms could move to varying degrees. Six participants experienced altered perception of where the phantom was in space or distortion of the phantom and one reported telescoping:

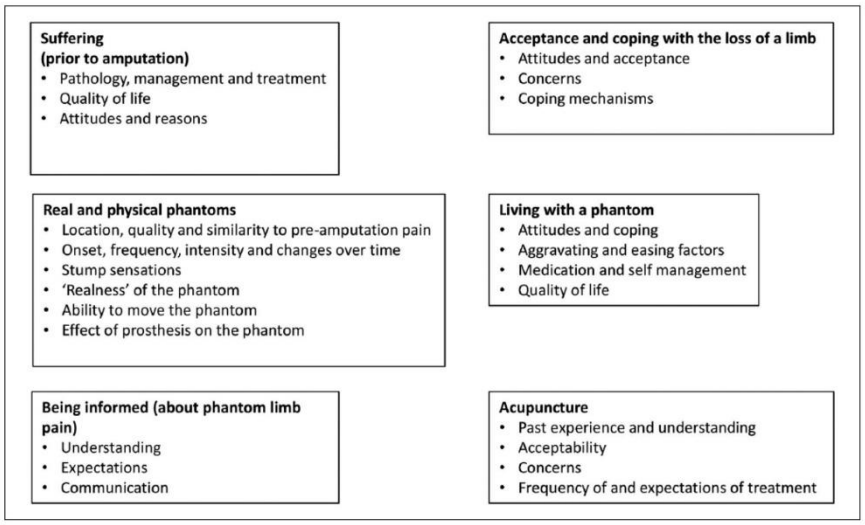

Figure 2. Key themes identified.

> I feel like I can open the toes and spread the toes … I can sit there and move the toes up and down and left and you know, I'm doing it now! (P12)

Living with a phantom

This theme describes attitudes towards PLP, effects of PLP on quality of life and management of PLP. These were grouped under one theme because they all described how PLP affected amputees on a daily basis. PLP was generally considered annoying/frustrating as pain was in a limb which was no longer present and was considered a constant reminder of circumstances:

> but it was so annoying. I mean how could I have a pain down there. It was so annoying! (P9)

> It's a constant reminder of what's happened. (P7)

However, four participants viewed PLP positively and did not necessarily want it to completely resolve, while others found it bizarre, weird and fascinating. PLP was viewed positively when it was considered better than the pre-amputation pain, when the amputee liked having sensations in the missing limb, when it was perceived as 'good pain' and when the amputee was glad just to be alive:

> it's just there, it's trying to tell me where my foot is, which is good. So, it's good pain if that makes sense. (P15)

> Makes me feel glad I'm alive really … As long as you are feeling something! (P6)

Approximately half of participants had disturbed sleep due to PLP. This impacted on performance in physiotherapy, mood, tiredness and decision-making. Most participants found PLP did not affect rehabilitation, and several found physiotherapy and wearing a pneumatic post-amputation mobility aid (PAMaid) helped:

> When I get there and they put on the balloon on the foot [PAMaid], it all goes. (P14)

Eleven participants reported PLP affected wellbeing or mood. PLP caused worrying, dark thoughts, depression, feeling 'miserable and down' and made participants act illogically and be withdrawn. Feelings could be mild 'sod this it's doing my head in' to severe:

> when it gets really bad I don't want to do anything. I don't want to eat, I don't want to do anything at all. I just want to be free of the pain. Um and if I was on the second floor of a building I'd probably want to jump out of the window because the pain just gets so much you can't cope with it. (P10)

PLP affected activities of daily living, state of mind and concentration and was considered tiring and wearing. Additionally, three participants reported PLP affected relationships:

> Cause you are in pain … you become irrational, you become snappy, you become less patient with people even though you may not have a reason for it. (P12)

Most frequently reported aggravating factors included lack of occupation, thinking about PLP and exercise, but exercise could both aggravate and ease symptoms. Distraction eased symptoms and a variety of techniques were employed, but participants were not always able to distract themselves:

> I was told by a couple of doctors that you should try and think about something else … and I've tried to get my mind on other things like reading the paper or looking at TV or whatever but I can't concentrate on it because this pain just kills it. (P10)

Stump techniques were used by six participants, including shaking the stump, rubbing/massaging the stump, hitting the stump. Medication was often not perceived as helpful or only helped for a number of hours. Only three participants had also been treated with non-pharmacological treatments (mirror therapy or graded motor imagery):

> they've said you are on as much medication as you can be on really and it's all the sort of stuff that helps hopefully treat phantom pain. It's not touching it yet. (P13)

Coping strategies involved acceptance of PLP. This was generally due to the feeling that because the pain was in a phantom limb, there was nothing that could be done.

Being informed

This theme describes participants' understanding of PLP and access to information. Generally, participants either expected or were not surprised to have PLP/PLS and expected it to resolve over time (years). These expectations often arose from speaking to other amputees. Participants had varied understanding of PLP. Participants generally expressed understanding that peripheral nerve damage due to amputation would result in pain. Cortical influences were always included in participant descriptions, but were not always scientifically grounded:

> You know if you cut through all of those nerves and those nerves still think there are feet and toes and there's legs there it's quite confusing for the nerves, very confusing for the brain. So it all makes sense why the pain is there. (P7)

Despite awareness of peripheral and cortical influences, views were expressed by three participants that mental state was a contributing factor or cause:

> I thought I won't get that. Idiots get that. I just thought its only mental people who get that … I just took it as a mental thing. (P8)

Participants generally felt there was lack of access to doctors, information provided was inadequate and did not come from the medical team. Only three participants were satisfied with the information provided. Participants/families had to seek out information. A number of resources were accessed, including the Internet, films and books. Families were sometimes needed to access and print out information:

> The only people who have explained it to me is other patients. But no doctors or nothing mentioned anything to me about the pain. (P9)

Discussion

The first theme described the physicality and realness of the phantom. Findings were consistent with other literature which reports that PLP is generally experienced in the distal portion of the limb[8] where there is the most extensive innervation density and cortical representation in the somatosensory cortex.[10] Some descriptions used to describe the quality of PLP were similar to other qualitative findings, giving a vivid picture of suffering emphasising the reality of the experience.

Exteroceptive perceptions experienced were similar to those described in other studies.[10] Telescoping was probably only experienced by one participant due to the short time frame between amputation and interview. As found in previous qualitative studies, kinetic perceptions were experienced and the amputated limb felt real and present. This may partly be due to changes in cortical representation in the somatosensory cortex and due to motor commands and the parietal lobe containing one's body image.[11] Increased awareness of the complexity of PLP and exteroceptive, kinetic and kinaesthetic sensations may improve understanding of the complexity of being an amputee.

The second theme discussed amputees' attitudes towards PLP, effects of PLP on quality of life and management of PLP. Unsurprisingly, PLP was often viewed as annoying, but it was not anticipated that some amputees would view PLP positively. It has been reported that a phantom and prosthetic can interlace into a single bodily structure and a phantom can aid the use of a prosthetic.[12] Awareness that PLP may be viewed positively and be wanted should be taken into account before trying to treat/resolve it.

Although not reported in other qualitative studies, sleep was frequently reported to be disrupted. A strong link exists between sleep and stress.[13] Insufficient sleep is associated with the development of chronic disease such as depression, diabetes, obesity and heart disease.[14] Amputation is in itself a stressful experience, and amputees often already have chronic conditions.

Poor sleep may exacerbate these factors as well as affecting performance and productivity.

PLP did not usually affect rehabilitation and some found wearing a PAMaid helped. This may be due both to rehabilitation acting as a form of distraction and because functionally effective prostheses can improve PLP.[15]

PLP affected wellbeing and mood. Pain and depressive symptoms commonly occur together, and chronic pain (⩾6 months) has been strongly associated with major depressive disorder. Ephraim et al.[3] found 28.7% of amputees had symptomatology of depression, and amputees with pain were more likely to have symptoms of depression than those without pain. Pain needs to be better managed to avoid the development of chronic pain and associated negative effects on wellbeing and mood.

Aggravating factors frequently included lack of occupation, thinking about PLP and exercise. Lack of occupation and thinking about PLP may cause emotionally triggered pain (exposure to isolated aspects of memories related to amputation revoke or worsen associated PLP[16]). Pain may also have been aggravated due to peripheral and central sensitisation,[17] disinhibition of pain mirror systems[16] and somatosensory maps and cortical reorganisation.[8] As found in other studies, distraction and stump techniques eased PLP. Distraction may help reduce emotionally triggered pain. Stump techniques may be effective through reducing muscle tension in the residual limb and through stump desensitisation.

Unsurprisingly, medication was not always effective. The efficacy of gabapentin from placebo-controlled trials is not robust. Amitriptyline and memantine are reported to not be effective, and the effectiveness of other medications remains unclear.[18] Mirror therapy and graded motor imagery may be effective interventions,[19] and amputees may benefit from improved access to these non-pharmacological alternatives.

The third theme described participants' understanding of PLP and access to information. Although participants generally did include descriptions of cortical and peripheral changes in their understanding of PLP, there were indications of a lack of thorough understanding. As found in previous studies, participants suggest there is a lack of provision of thorough patient education about PLP. Neuroscience education can decrease pain ratings, increase physical performance and decrease perceived disability and catastrophising in musculoskeletal patients.[20] This approach could be used to educate amputees about PLP.

Limitations

Credibility may have been reduced due to the researcher not being able to spend prolonged periods of time with amputees or being a 'member of the group'. However, lack of prolonged engagement may encourage openness. The research did not include formal member checks (findings are presented to participants) or referential adequacy (a portion of data is archived and post development of preliminary findings is analysed to test validity of these findings), but member checking is disputed due to ethical reasons and because participants may have changed their viewpoint over time. The purposive quota was not completely met, so reducing transferability of findings. Differences in gender, ethnicity and level of amputation were not explored in this study. Lack of methodological triangulation may make results less creditable and confirmable. Although the research was not audited, it was transparent and all steps during the research process were recorded to ensure it was auditable. The sample size was small, and determining whether theoretical data saturation had been met was challenging. However, as no new concepts emerged in the final interviews, it was considered achieved. Future studies may benefit from having a more homogenous sample. This sample may not be representative of all those with PLP, but this could be researched further.

Conclusion

Findings provide insight for clinicians on the lived experience of PLP. Numerous painful 'real' qualities are experienced with PLP, and descriptions depict suffering. PLP is a continual reminder of circumstances and can affect quality of life including sleep, fatigue mood and relationships. This should be considered clinically during therapeutic encounters, and amputees should be given appropriate information on these potential associations. Phantoms can feel real, with kinetic and kinaesthetic properties. There is still a perception that PLP is due to mental state, and education needs to be improved to help both patient understanding and management of PLP. The study has identified the need for future research to gain insight into the educational needs of amputees and to evaluate the awareness and accessibility of non-pharmacological interventions which have evidence of effectiveness.

Acknowledgements

Many thanks to the clinical staff at the Amputee Rehabilitation Unit, Lambeth Community Care Centre, London, for their help with the running of this study. Also, thanks to all participants who took part in the study. The study was completed as part of a PhD at London South Bank University (LSBU).

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Appendix 5.2 Participant information sheet for qualitative descriptive study

London South Bank University

Guy's and St Thomas' NHS
NHS Foundation Trust

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INFORMATION SHEET

ACUPUNCTURE IN THE TREATMENT OF PHANTOM LIMB SYNDROME

NHS Ethics number: 13/EE/0313 University Ethics number: UREC1361
Version number: 02 Date: 10.10.2013
Name of Researcher: Esme Trevelyan

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. The researcher will go through the information sheet with you and answer any questions you have. This should take about 20 minutes. Talk to others about the study if you wish.

(Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study). Ask us if there is anything that is not clear.

Part 1

What is the purpose of the study?
Phantom limb syndrome is sensations and / or pain in a missing limb. It is not pain in the remaining stump.
The aim of this study is to understand if acupuncture would be an acceptable method of treatment for phantom limb syndrome. The study aims to discover how you would feel about receiving acupuncture and whether you would be happy to receive acupuncture in various parts of your body (such as your stump, remaining limb etc.). The study also aims to establish measurements which you would consider appropriate to measure phantom limb syndrome. This information will help us to decide on acupuncture protocols and measurements which we will then use in further research in this area.

Why have I been invited?
You have been chosen to participate in this study if you are:

- 18 years of age or above
- Able to communicate in English (written and verbal)
- An inpatient at the Amputee Rehabilitation Unit
- A lower limb amputee
- Currently have or have suffered in the past from phantom limb syndrome. (This is pain / sensations in your missing limb. It is not pain which is only in your stump. It may however present as pain / sensation in both your stump AND your missing limb).

Do I have to take part?
It is up to you to decide whether or not to take part. We will describe the study and go through the information sheet with you. If you agree to take part, we will then ask you to sign a consent form. You are still free to withdraw at any time, without giving a reason. A decision to withdraw or decision not to take part will not affect the standard of care you receive.

What will happen to me if I take part?
If you are willing to participate, you will be invited to attend in an interview with the researcher. The interview will take place in your room at the Amputee Rehabilitation Unit whilst you are an inpatient here. The interview will last approximately 1 hour and will be arranged at an agreeable date and time to suit you. During the interview, the researcher will explore with you your thoughts on having acupuncture to treat phantom limb syndrome. The researcher will ask how you feel about having different parts of your body acupunctured (such as your stump and other leg). The researcher will also show you some different assessment questionnaires commonly used to assess problems like phantom limb syndrome and ask for your feedback on whether you feel they are appropriate. For accuracy of information the interview will be tape recorded as well as notes taken during the interview.
You will only be asked to give one interview. You will however, also be asked to read a transcript of your interview (approximately one week post interview) to ensure accuracy of information. You will therefore be involved in the study for 1-2 weeks in total. The overall study is planned to last approximately 6 months.

Any published work from the interviews may contain direct quotes from your interview but these will be recorded using a numerical code.

Expenses and payments
This study is being undertaken with no funding so no expenses will be given for your time.

What will I have to do?
You will be required to attend one interview whilst you are an inpatient at the Amputee Rehabilitation Unit at a time convenient to you. You will also be asked to read a transcript of your interview 1-2 weeks post interview to check you are happy with the content.

What are the possible disadvantages and risks of taking part?
It is not anticipated that there are any risks associated with this study. The interview should not be distressing or cause any emotional upset. However, some people do find talking about their pain / symptoms distressing and it is important you are aware of this.

What are the possible benefits of taking part?
It is unlikely that you will gain any personal benefit from participating in this research. However, the information you share with the researcher will help with the development of acupuncture protocols for the treatment of phantom limb syndrome. Some people gain some benefit from having the opportunity to discuss their opinions with a receptive listener.

What if there is a problem?
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes part 1.
If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2

What will happen if I don't want to carry on with the study?
You are free to withdraw from the study and not have your information included, at any time up to the time of completion of this study. However, after that time, it would be impossible for us to comply.
Regardless of whether you participate or not in the study, if it is clinically indicated you will have the opportunity to be referred for acupuncture while under the care of Lambeth Community Care Centre.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with the researcher who will do their best to answer your questions (Esme Trevelyan: tel: 07768 348407 email: trevelye@lsbu.ac.uk). If you wish any further information regarding this study or have any complaints about the way you have been dealt with during the study or other concerns you can contact the director of studies: Prof Nicola Robinson at London South Bank university; tel: 0207 815 7940, who is the Academic Supervisor for this study. Finally, if you remain unhappy and wish to complain formally, you can contact PALS. Tel: 020 7188 8801 or 020 7188 8803. Email: pals@gstt.nhs.uk or the Chair of the University Research Ethics Committee (email ethics@lsbu.ac.uk). Details can be obtained from the university website: https://my.lsbu.ac.uk/page/research-degrees-ethics

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against London South Bank University who are the sponsors of the study but you may have to pay your legal costs.

Will my taking part in this study be kept confidential?
This study is being completed as part of a MPhil / PhD degree at London South Bank University. It has been reviewed and ethically approved by the London South Bank University Research Ethics Committee and the National Health Service Research Ethics Committee. All information received from you will be handled in a confidential manner. If you join the study, some parts of the data collected for the study will be looked at by authorised persons from London South Bank University. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty under the Data Protection Act of confidentiality to you as a research participant and we will do our best to meet this duty. All information will be stored in a locked filing cabinet and on a password protected computer in an environment locked when not occupied. Any reference to you will be coded. This information will be held for 5 years before being disposed of securely. Data will not be retained for the use in future studies.

What will happen to the results of the research study?
Results of the study will be made available to you if you so wish and you will be invited to give any feedback to us about the results of the study. If you do wish to receive the results of the study we will send them to you when they become available.

The research may be published. Any published work will use a numerical code to protect your identity.

Who is organising and funding the research?
The research is unfunded as it is an educational project.

Who has reviewed the study?
All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by London - Brent Research Ethics Committee.

Further information and contact details
If you need further general information about research, specific information about this project or advice on participation please contact Esme Trevelyan (tel: 0207815 8349. Email: trevelye@lsbu.ac.uk)

Appendix 5.3 Participant consent form for qualitative descriptive study

London South Bank University

Guy's and St Thomas' NHS
NHS Foundation Trust

Esme Trevelyan
Faculty of Health and Social Care
London South Bank University
103 Borough Road
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Amputee Rehabilitation Unit
Lambeth Community Care Centre
Monkton Street
London
SE11 4TX

Tel: 0203 0496912

CONSENT FORM

ACUPUNCTURE IN THE TREATMENT OF PHANTOM LIMB SYNDROME

Ethics number: 13/EE/0313 University Ethics number: UREC1361
Version number: 02 Date: 18.11.2013
Name of Researcher: Esme Trevelyan
Patient Identification Number for this study:.....

	Please initial the box
I confirm that I have read and understand the information sheet dated 10.10.2013 (version 02) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	
I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected.	
I understand that relevant sections of data collected during the study, may be looked at by individuals from London South Bank University, from regulatory authorities or from Guy's and St Thomas' NHS Foundation Trust. I give permission for these individuals to have access to my records.	
I consent to use of audio-taping during the interview with possible use of verbatim quotations in the research project	
I agree to give feedback on the transcribed interview to confirm I am happy with the content	
I agree to take part in the above study	

Name of patient	Date	Signature
Researcher	Date	Signature

Appendix 5.4 Interview topic guide for qualitative descriptive study

Interview Topic Guide

Date of interview:……..

Study ID number:……..……

Demographics

1. Age in years
2. Gender
3. When did you leave school or full time education? Education level achieved
4. Marital status
5. Living alone or with partner / sheltered / supported housing
6. Occupation / employment status

General Health

1. Do you take any medication, if so what and what for
2. Do you have any other health conditions e.g. diabetes, high blood pressure

Amputation History

1. Date of most recent amputation
2. Level of most recent amputation
3. Reason for most recent amputation
4. Any previous amputations

Mobility Levels

1. Mobility prior to most recent amputation
2. Mobility post most recent amputation (prosthesis / sticks/ ZF / transfers)

Pain History

1. Pain prior to amputation in amputated limb
2. Pain post amputation in amputated limb (stump pain and / or phantom limb sensation)
3. Current pain / sensations in amputated limb (description and location and intensity)
4. Frequency and duration of any current pains / sensations in amputated limb
5. Is current pain / sensations in amputated limb getting better, worse or staying the same
6. What aggravates / eases any current pain / sensation in amputated limb
7. Is pain worse at night or during the day – does it wake you up at night

Pain Interventions

1. Past and current treatments / interventions used for any general pain relief and their effectiveness
2. Past and current treatments / interventions used for pain / sensation in amputated limb and their effectiveness
3. What other sort of pain relief would you try
4. What do you think is causing the pain in your missing limb

Acupuncture

1. Any past experience of any form of complementary medicine e.g. reflexology, herbal medicine
2. Past experience of acupuncture
3. Understanding of how acupuncture works and whether you feel it is important to understand how it works
4. Willingness to try acupuncture
5. Fear of needles
6. Concerns about receiving acupuncture (pain, adverse effects, harm)
7. Acceptability of receiving acupuncture in different parts of body (head, ear body and leg)
8. Acceptability of receiving electro-acupuncture
9. Willingness to receive specific types of acupuncture if research had shown it to be effective
10. How often would you be prepared to have acupuncture in addition to your conventional treatment and rehab – any particular time of day be more appropriate

Research / Outcome measures

1. How would you feel about taking part in a research study evaluating the effectiveness of acupuncture for treating phantom limb syndrome during your stay at the Amputee Rehabilitation Unit
2. Participants to be shown outcome measures and asked how they feel about:
    a. Ease of completion
    b. Can they understand them
    c. Are they relevant to their pain / sensation in their amputated limb and their current general health
    d. Is there anything else they feel they should have been asked
    e. Acceptability of time it takes to complete outcome measures

The following outcome measures will be shown to participants:

a. NRS to gain feedback on measuring pain intensity
b. SF-MPQ-2, NPS and NPSI to gain feedback on which is preferred for measuring quality of pain
c. EQ-5D-5L and BPI to gain feedback on which is preferred for measuring physical functioning / quality of life
d. HADS to gain feedback on measuring emotional function
e. ISI to gain feedback on measuring sleep
f. PGIC to gain feedback on measuring ratings of improvement

Appendix 5.5 Ethical approval letter from NRES Committee London – Brent, and London South Bank University for qualitative descriptive study

London South Bank University

Direct line: 020-7815 6025 E-mail: mitchen5@lsbu.ac.uk
Ref: UREC 1361

Esme Trevelyan
London Southbank University
Faculty of Health and Social Care
London South Bank University
103 Borough Road
SE1 0AA

Thursday 21 November 2013

Dear Esme,

Re: An evaluation of the acceptability of acupuncture as an intervention for phantom limb syndrome in lower limb amputees; a qualitative study

Thank you for submitting this proposal and for your response to the reviewers' comments.

I am pleased to inform you that Full Chair's Approval has been given by Vice Chair on behalf of the University Research Ethics Committee.

I wish you every success with your research.

Yours sincerely,

Nicola Mitchell

Secretary, LSBU Research Ethics Committee

cc:
Prof Shushma Patel, Chair, LSBU Research Ethics Committee

Health Research Authority

NRES Committee London – Brent
80 London Road
Skipton House
London
SE1 6LH

Telephone: 020 7972 2552

20 November 2013

Prof Nicola Robinson
Professor of Traditional Chinese Medicine (TCM) and
Integrated Health London Southbank University
Faculty of
Health and
Social Care
London South
Bank University
103 Borough
Road
SE1 0AA

Dear Professor Robinson

Study title: An evaluation of the acceptability of acupuncture as an intervention for phantom limb syndrome in lower limb amputees; a qualitative study.

REC reference: 13/LO/1409
IRAS project ID: 136298

Thank you for your letter of 18th November 2013. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 07 October 2013

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Covering Letter		18 November 2013
Participant Consent Form	2	18 November 2013
Protocol	3	08 November 2013

Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	*Version*	*Date*
Covering Letter		16 August 2013
Covering Letter		18 November 2013
Evidence of insurance or indemnity		16 August 2013
Interview Schedules/Topic Guides	1	16 August 2013
Investigator CV		16 August 2013
Letter from Sponsor		16 August 2013
Other: Summary CV for Supervisor		16 August 2013
Other: Summary CV for Student		16 August 2013
Participant Consent Form	2	18 November 2013
Participant Information Sheet	02	10 October 2013
Participant Information Sheet	02	10 October 2013
Protocol	02	10 October 2013
Protocol	02	10 October 2013
Protocol	3	08 November 2013
REC application	1	16 August 2013

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

13/LO/1409 **Please quote this number on all correspondence**

Yours sincerely

Ms Julie Kidd
Committee Co-ordinator

E-mail: Juliekidd@nhs.net

Copy to: *Prof Nicola Crichton,*
Ms Rachel Fay, Guy's And St Thomas' NHS Foundation Trust

Appendix 6.1 Published paper of feasibility study protocol

Trevelyan *et al. Trials* (2015) 16:158
DOI 10.1186/s13063-015-0668-3

TRIALS

STUDY PROTOCOL Open Access

Acupuncture for the treatment of phantom limb pain in lower limb amputees: study protocol for a randomized controlled feasibility trial

Esmé G Trevelyan*, Warren A Turner and Nicola Robinson

Abstract

Background: Phantom limb pain is a prevalent condition that is difficult to manage, with a lack of robust evidence to support the use of many adjunctive treatments. Acupuncture can be effective in the management of many painful conditions but little is known about its effectiveness in treating phantom limb pain. The aim of this study is to explore the feasibility of conducting a randomized controlled trial comparing acupuncture and routine care in a group of lower limb amputees with phantom limb pain.

Methods/design: An unstratified, pragmatic, randomized, two-armed, controlled trial of parallel design comparing acupuncture and usual care control will be conducted. A total of 20 participants will be randomly assigned to receive either usual care or usual care plus acupuncture. Acupuncture will include eight 1 hour treatments delivered pragmatically over 4 weeks by practitioners trained in traditional Chinese medicine. As outcome measures, the Numerical Pain Rating Scale, short-form McGill Pain Questionnaire 2, EQ-5D-5 L, Hospital Anxiety and Depression Scale, 10-Item Perceived Stress Scale, Insomnia Severity Index, and Patient Global Impression of Change will be completed at baseline, weekly for the duration of the study and at 1 month after completion of the study. After completion of the trial, participants will provide feedback though semi-structured interviews.
Feasibility will be determined through the ability to recruit to the study, success of the randomization process, completion of acupuncture intervention, acceptability of random allocation and completion of outcome measures. Acceptability of the acupuncture intervention will be determined through semi-structured interviews with participants. The appropriateness of outcome measures for a future trial will be addressed through completion rates of questionnaires and participant feedback.

Discussion: Data generated on effect size will be used for future sample size calculations and will inform the development of an appropriate and feasible protocol for use in a definitive multicentre randomized controlled trial.

Trial registration: ClinicalTrials.gov: NCT02126436.

Keywords: Acupuncture, feasibility studies, pain, phantom limb

Background

Phantom limb pain, defined as painful sensations perceived in the missing portion of the amputated limb [1], was recorded medically as early as the sixteenth century by Ambroise Paré [2]. It is very common and prevalence may be as high as 75 to 80% [3,4].

Treatment of phantom limb pain includes such interventions as pre-emptive analgesia, pharmacological interventions, neuromodulation and supportive non-pharmacological or noninvasive techniques, such as mirror therapy, graded motor imagery and stump liners. Evidence suggests that pre-emptive epidural and perineural analgesia might not prevent chronic phantom limb pain [5,6]. Pre-emptive gabapentin has also been found to be ineffective [7]. Pharmacological interventions, including morphine, gabapentin and ketamine, may provide short term analgesic efficacy [8]. There is a lack of robust evidence to support the use of neuromodulation [9], mirror therapy [10] or

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graded motor imagery [11]. One randomized controlled trial suggested that stump liners might reduce phantom limb pain [12] but the sample size in this study was small.

Acupuncture has been shown to be an effective intervention in the management of many pain conditions [13-15] but little is known about the effectiveness of acupuncture for the treatment of neuropathic pain [16]. Specifically, the effectiveness of acupuncture for treating phantom limb pain has not been widely assessed or documented, with most of the literature consisting of case reports [17,18]. Although these studies generally report positive outcomes [17], they are at the bottom of the hierarchy of evidence [19]. A systematic review including English, Chinese and Korean databases identified only two nonrandomized controlled trials evaluating the effectiveness of acupuncture. Although these studies reported positive outcomes, both were deemed to have a high risk of bias and low methodological quality [20]. Further research is needed to evaluate the effectiveness of acupuncture for treating phantom limb pain but, prior to a definitive trial, a study is needed to determine feasibility [21].

The objectives of this study are to: (1) explore the feasibility of recruiting, randomizing and retaining participants; (2) evaluate the feasibility and acceptability of including a standard care control; (3) evaluate the adherence or compliance and acceptability of acupuncture as an intervention; (4) evaluate the appropriateness of outcome measures and their completion rates and explore participants' experience in completing outcome measures; (5) identify appropriate primary and secondary outcome measures that could be used in future trials; (6) explore the perceived effectiveness of acupuncture in treating phantom limb syndrome; (7) generate data on effect size for use in future sample size calculations; and (8) inform the development of an appropriate and feasible protocol for use in a definitive multicentre randomized controlled trial.

Methods/design

Design

A comparative effectiveness feasibility study will be conducted, using a mixed-methods approach, including a small randomized controlled trial and semi-structured interviews. The randomized controlled trial will be an unstratified, open, pragmatic, effectiveness trial, of parallel design, with two arms, using balanced randomization between acupuncture and usual care and a usual care control. Cross-sectional interviews will be carried out at the end of the intervention period.

Ethical approval was granted from the National Research Ethics Service Committee London (Bloomsbury) in July 2014 and Guy's and St Thomas' R & D and London South Bank University in October 2014. The trial is registered with ClinicalTrials.gov (NCT02126436) https://www.clinicaltrials.gov/ct2/show/study/NCT02126436 and will be conducted in compliance with the principles of the Declaration of Helsinki [22] the London South Bank University Code of Practice, and the London (Bloomsbury) Research Ethics Committee.

Study settings

The study will be conducted at the Amputee Rehabilitation Unit, at Lambeth Community Care Centre, London, Guy's and St Thomas' NHS Foundation Trust. The Amputee Rehabilitation Unit is a 12-bed inpatient unit that provides specialist rehabilitation after major amputation. It accepts both primary and established amputees who have undergone a functional decline for approximately 7 weeks of evidence-based care, including access to specialist medical, nursing, therapy, and counselling professionals. Acupuncture will be provided at the Gateway Acupuncture Clinic (which is located in the same building) and provides an NHS acupuncture service through GP referral, in the area of Lambeth and Southwark. The clinic provides treatment for chronic long-term conditions, specializing in chronic pain, headaches, migraines and HIV.

Recruitment

Participants will be approached and recruited whilst they are inpatients at the Amputee Rehabilitation Unit. Newly admitted potential participants will be identified by clinical staff (JG, CC), approached by the researcher (EGT), initially screened, and provided with oral and written information. Participants who pass initial screening tests and are willing to participate will have a final eligibility check by EGT before enrolment in the study (Figure 1). Signed, informed consent will be obtained from all participants before enrolling them in the study. Those declining to participate will be asked briefly for their reasons. As the study is a feasibility study, no sample size calculation has been performed [21]. An arbitrary number of 20 participants was deemed adequate to provide information on recruitment, randomization and acceptability of acupuncture and answer the objectives of this trial [23].

Eligibility criteria

Participants will be included if they: (1) at least 18 years of age, (2) have full cognitive ability and are able to communicate in English, (3) have traumatic or medical amputation of a lower limb (greater than toes), and (4) are currently experiencing phantom limb pain of ≥5 on an 11-point verbal rating scale (that is, moderate or severe phantom limb pain) [24]. Participants will be excluded if they: (1) have congenital limb absence, (2) are medically too unwell (as advised by medical staff at the Amputee

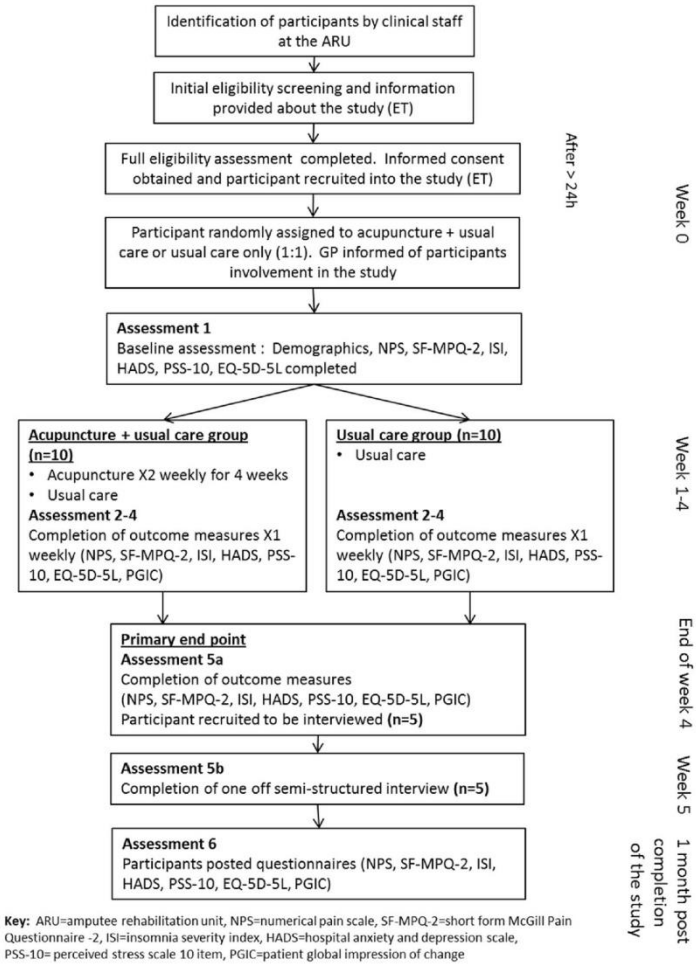

Figure 1 Participants' flow through the study. The different phases of the study and participants' flow through the study with details on timings of the different phases of the study. ARU, Amputee Rehabilitation Unit; GP, general practitioner; HADS, Hospital Anxiety and Depression Scale; ISI, Insomnia Severity Index; NPS, numerical pain scale; PGIC, Patient Global Impression of Change; PSS-10, 10-Item Perceived Stress Scale; SF-MPQ-2, short-form McGill Pain Questionnaire 2.

Rehabilitation Unit), (3) are pregnant, or (4) where acupuncture is cautioned, including participants with poorly controlled epilepsy, severe haemophilia or other bleeding or clotting disorders, or a pacemaker (if using electro-acupuncture), and patients undergoing or who have recently undergone chemotherapy or bone marrow transplant, any skin changes or removal of lymph nodes in the body, that would preclude placement of acupuncture needles [25].

Intervention (RCT)

The acupuncture group (group A) will receive usual inpatient care and a course of acupuncture. The control group (group C) will receive usual inpatient care only. Usual care will include both medical intervention and daily physiotherapy and rehabilitation, as routinely provided at the Amputee Rehabilitation Unit.

All acupuncture practitioners involved in the study will be trained in the practice of traditional Chinese

medicine. All practitioners will be members of the British Acupuncture Council, will have at least 15 years clinical experience and will follow the safety guidelines of the British Acupuncture Guide to Safe Practice [25]. Acupuncture needles will be single-use, presterilized, disposable, solid, stainless steel needles (with prepacked single-use guide tubes if guide tubes are used). The acupuncture intervention will be pragmatic but will be guided by a protocol previously developed though a Delphi practitioner consensus study [26]. This protocol advises:

- Using a combination of body and auricular acupuncture;
- Treating the contralateral limb and possibly the ipsilateral limb;
- Including auricular acupuncture points such as shen men, sympathetic and points corresponding to the lower limb;
- Depending on the health of the tissue and the individual participant, needling around the stump;
- Mirroring local and distal points by needling the opposite limb;
- Including points on the lower back (taking a segmental approach to dermatomal pain);
- Including points such as LI4 + LR3, LR3, GV20, SP10 and also specified points according to participants' specific symptoms;
- Retaining needles for 20 to 30 minutes.

No set criteria will be followed when needling, other than to follow the guidelines of the protocol. Practitioners will assess and treat participants under the paradigm of traditional Chinese medicine. Treatment may (depending on the practitioner's diagnosis and treatment plan) include electro-acupuncture or other adjunctive interventions, such as cupping. All participants in group A will receive eight one-hour acupuncture sessions (twice weekly for 4 weeks) delivered during their inpatient stay.

Withdrawals, discontinuation and post-trial care

Acupuncture is a low-risk intervention and any adverse effects are usually minimal and temporary. In the event of mild adverse effects (drowsiness, haematoma, bleeding from a point, stuck needle, pain after needling a point) participants will not be withdrawn but will be able to drop out if they so wish. In the event of the occurrence of more serious adverse events, participants will be withdrawn. As evidence suggests that acupuncture is a safe treatment [27,28] and as this study is not assessing effectiveness, no specific arrangements have been made to review interim safety and effectiveness. However, in the event of three participants reporting prolonged aggravation of pain or other potential serious adverse events, the trial will be stopped prematurely. After completion of the study, participants will be offered access to acupuncture through their general practitioner or physiotherapist.

Concomitant care

Participants will be asked to refrain from using other forms of complementary therapy for the duration of the trial but may receive any intervention as routinely prescribed by clinical staff at the Amputee Rehabilitation Unit.

Study restrictions

Participants and practitioners will be asked not to disclose participant allocation to the researcher (EGT).

Intervention (interviews)

Consecutive sampling will be used to recruit ($n = 5$) participants from group A to explore their experience of being in the trial, having acupuncture and completing outcome measures. Participants will be interviewed once after completion of the study. Semi-structured interviews will be facilitated by EGT, will follow a topic guide (Additional file 1) and will be recorded and transcribed verbatim.

Randomization, allocation concealment and blinding

Randomization and allocation concealment will be used to ensure against selection bias [29]. Prior to commencement of the study, a researcher (NR) not involved in the day-to-day execution of the study will randomly allocate and conceal allocation. A copy of the randomized sequence will be kept in a locked cabinet and not shared with study personnel. The researcher (EGT) who will enrol participants and assign them to either acupuncture intervention or control will not know the random sequence or treatment allocation.

Randomization will be achieved using a computer-generated random numbers table and will be unstratified and balanced (1:1). Permuted blocking will be used to achieve balance between study arms. A block size of four will be used in this study. Allocation concealment will be implemented using sequentially numbered, opaque sealed envelopes. The envelopes will be opened sequentially only after participant's details are written on each envelope.

Participants and practitioners involved in the study will not be blinded. However, the researcher collecting outcome measures (EGT) will be blind to the participant's allocation.

Outcome measures

Recommendations from the Assessment Committee of the Neuropathic Pain Special Interest Group [30] and the Initiative on Methods, Measurements, and Pain Assessment

in Clinical Trials [31] were taken into consideration when developing outcome measures for use in this trial.

The primary outcome measure will be an 11-point numerical rating scale to record pain intensity. Pain will be rated by a number describing average pain over the previous week, using the anchors 0, meaning 'no pain', and 10, meaning 'pain as bad as you can imagine' [31]. The numerical rating scale is an appropriate measure of pain intensity [32] and is a recommended outcome measure for clinical trials of chronic pain treatment effectiveness [31].

Secondary outcome measures will include a numerical rating scale measuring 'worst' pain, the short-form McGill Pain Questionnaire 2 (SF-MPQ-2), EQ-5D-5 L, Hospital Anxiety and Depression Scale, 10-Item Perceived Stress Scale, Insomnia Severity Index, and Patient Global Impression of Change.

The McGill Pain Questionnaire and its short form (SF-MPQ) are generic questionnaires (applicable to any pain), whose reliability and validity have been extensively documented [33]. The SF-MPQ-2 is a 22-item questionnaire that uses a 10 point rating scale and records the major symptoms of both neuropathic and non-neuropathic pain [34]. It is reliable and valid for measuring diverse chronic pain [35].

The EQ-5D measures health-related quality of life and although not validated for use in neuropathic trials, results appear robust in neuropathic trials with a large sample size or when recording a large-pain relief response in the active group [30]. The EQ-5D-5 L has the same core dimensions as the EQ-5D but instead of a three-point rating scale it uses five levels.

The Hospital Anxiety and Depression Scale measures emotional function and is responsive to change in neuropathic pain clinical trials [30]. It includes seven depression and seven anxiety items to cover cognitive and emotional aspects of depression and anxiety and is reliable and valid for assessing emotional distress in a medical population [36].

The Perceived Stress Scale is a 4-, 10- or 14-item questionnaire that was designed to measure psychological stress [37]. It is reliable and valid and was found to have acceptable psychometric properties across 19 studies [38]. The 10-item version has no loss of psychometric quality, compared with the 14-item version [39] and has, in fact, been shown to be superior [38].

The Insomnia Severity Index measures perception of insomnia and the degree of concerns or distress caused by insomnia; it consists of seven items [40]. It has the advantage of measuring symptoms over a 2-week period and is recommended when insomnia is a secondary endpoint. It has been validated against both polysomnographic and prospective sleep diary measures [40,41].

The Patient Global Impression of Change scale is advised for use in clinical trials [30,31] and provides a readily interpretable assessment of participants evaluation of the importance of their improvement [42]. The scale used in this study will be a seven-point scale that ranges from 'no change or worse' to 'a great deal better' [43].

Assessment

Participants will complete the questionnaires and rating scales six times in total. Data for all items (except the Patient Global Impression of Change, data for which will only be collected from the end of week one) will be collected at the time of enrolment and at the end of each week for the duration of the study. The primary endpoint will be at the end of the intervention (end of week 4). Data for the outcome measures will also be determined one month after completion of the study. Questionnaires and rating scales will be completed under the supervision of the researcher (EGT) at baseline and during weeks 1 to 4 (whilst participants are inpatients at the Amputee Rehabilitation Unit), and will be posted to participants one month after completion of the study.

Analysis

As this is a feasibility study, emphasis will be on feasibility and not on statistical significance of results [21]. Compliance with the protocol will be examined through number counts on drop outs or numbers of missed treatments, completion rates of outcome measures, and their perceived appropriateness and deviation from the protocol. Data will be collected on the use of rescue medication and adverse events (captured through open-ended prompts by practitioners at each intervention time point). Details of any participants who are excluded from the study will be reported and exclusion will be distinguished from attrition.

All statistical analysis will be undertaken using SPSS Version 21 software. The analysis will test for within-patient and between-group differences in measurements taken at the beginning of the study, during the study, at the end of the study and one month after completion of the study. An intention-to-treat approach will be taken [44]. To include missing data, any missing data will be imputed using the last observation carried forward [45].

The null hypothesis is that there is no difference in change in the primary outcome measure between group A and C at the end of intervention (end of week 4). Statistical analysis will be performed to verify rejection of the null hypothesis with a $P = 0.05$ taken as indicative of statistical significance. Nonparametric tests will be used in inferential analysis. The nonparametric Mann–Whitney U test will be used for analysis between groups. The difference between baseline and last observation scores will be analyzed using Wilcoxon signed-rank test. The effect size (Cohen's d) will be calculated to provide information on the relative magnitude of

difference [46]. All secondary outcome measures will be treated in the same way as the primary outcome. Categorical and continuous baseline characteristics will also be analyzed to test for between-group differences.

A framework analysis procedure [47] will be used to analyze qualitative data. NVivo 10 software will be used to develop the analytic framework and index transcripts. Microsoft Excel will be used during charting. Interviews will be transcribed verbatim. Specific steps will be followed during data analysis, including; familiarization, coding, identifying an analytic framework, indexing, charting and mapping or interpretation. To ensure credibility, peer debriefing will take place throughout the research process. To ensure dependability, two researchers will separately code a selection of transcripts.

The trial will be considered successful if:

- Recruitment rate is ≥2 participants per month fitting the eligibility criteria.
- The study recruits ≥70% of all eligible potential participants.
- Of the participants recruited to group A, ≥90% receive their first acupuncture treatment within one week of recruitment.
- After randomization and allocation, ≥90% of participants receive treatment as initially intended.
- Of the participants recruited to group A, ≥80% receive all eight acupuncture treatments.
- Of the participants recruited to group C, ≤10% drop out of the study.
- At the primary endpoint of the study, questionnaires and rating scales for outcome measures are completed by ≥90% of participants.
- At one month after completion of the study, questionnaires and rating scales for outcome measures are completed by ≥60% of participants.
- Qualitative data identifies that outcome measures are acceptable and appropriate, that questionnaires and rating scales are easy to complete and that outcome measures can be identified for used in a definitive trial.
- Qualitative data implies that acupuncture is an acceptable and effective intervention for treating phantom limb pain with or without other secondary symptoms.
- Qualitative and quantitative data implies that the acupuncture protocol used in the feasibility study is appropriate for use in a definitive multicentre randomized controlled trial.

Data management and reporting

The Consolidated Standards of Reporting Trials (CONSORT) [48] and Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA) [49] will be adhered to when reporting. Data will be stored securely with no participant identifiers included. Access to and handling of data will be restricted to those involved in the study. All disseminated findings will contain no participant-identifiable data.

Discussion

Currently, no genuine placebo-controlled acupuncture trials exist [50]. Different types of sham acupuncture have been implemented in acupuncture trials, including; shallow needling of acupuncture points, using nonpenetrating needles, needling non-acupuncture points and needling acupuncture points that are not indicated for that specific condition, but none of these methods is physiologically inert [50] and sham acupuncture might have some level of effectiveness [51]. Therefore, despite a lack of blinding introducing ascertainment bias, sham acupuncture will not be used in this study and will not be used in a future definitive trial.

Inferential statistical analysis and hypothesis testing will be completed only to pilot procedure and will not be interpreted as a measure of effectiveness of acupuncture. Effectiveness will only be established after completion of a fully powered randomized controlled trail.

Results of this study will be disseminated through publication.

Trial status

Recruitment commenced in October 2014 and it is anticipated that it will finish by October 2015.

Additional file

Additional file 1: Summary of the interview topic guide. This guide will be used to interview participants in the acupuncture group after completion of the randomized controlled trial. PLP, phantom limb pain.

Abbreviation

SF-MPQ-2: short-form McGill Pain Questionnaire 2.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

EGT, WAT and NR designed the study. EGT will enroll participants, and will collect and analyze data. NR and WAT will review quantitative data analysis. Qualitative data coding will be reviewed and discussed by WAT and NR, and NR will act as a second coder, coding a portion of the data using the analytic framework. EGT drafted the manuscript. All authors read and approved the final manuscript.

Authors' information

EGT is both a chartered physiotherapist (BSc Physiotherapy) and an acupuncturist (MSc Chinese Medicine) and is currently completing a PhD at London South Bank University. NR completed a PhD in 1976, has been a licensed traditional Chinese medicine acupuncturist since 1982, and is a professor of Chinese Medicine and Integrated Health at London South Bank University. WAT is a podiatrist; he completed a PhD in 2001 and is Pro Vice Chancellor and Dean of the School of Health and Social Care at London South Bank University.

The trial sponsor is London South Bank University. The contact person for the trial is Prof Nicola Crichton, Faculty of Health and Social Care, London South Bank University. The sponsor had no role in the collection, management, analysis, and interpretation of data; writing of the report or the decision to submit the report for publication.

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Appendix 6.2 Participant information sheet for feasibility study

London South Bank University

A CATALYST FOR INNOVATION IN HEALTH

GUY'S & ST THOMAS' CHARITY

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INFORMATION SHEET

Acupuncture for the treatment of Phantom Limb Syndrome 2

REC Ethics number: 14/LO/0817
Version number: 02 Date: 11.06.2014
Name of Researcher: Esmé Trevelyan

We would like to invite you to take part in our research study. Before you decide we would like you to understand why the research is being done and what it would involve for you. The researcher will go through the information sheet with you and answer any questions you have. This should take about 20 minutes. Talk to others about the study if you wish.

(Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study). Ask us if there is anything that is not clear.

Part 1

What is the purpose of the study?
Phantom limb syndrome is sensations and / or pain in a missing limb. It is not pain in the remaining stump.
The aim of this study is to evaluate if acupuncture would be a feasible method of treating phantom limb syndrome. The study aims to assess the feasibility of using acupuncture as compared to the routine care you receive at the Amputee Rehabilitation Unit and evaluate the acceptability of using acupuncture. Data collected will measure whether acupuncture is helpful in reducing your pain and other symptoms. Pain can stimulate a natural stress response which produces a hormone called cortisol. It has been found that individuals have natural genetic differences in the part of the body that detects this hormone. We would like to know if these natural differences correspond to personal response to pain. We will also explore your experience of being part of the study and completing questionnaires.
The information from this preliminary study will help us devise acupuncture protocols to use in future trials designed to evaluate if acupuncture is effective. This preliminary study should be followed by a larger scale study which will specifically evaluate the effectiveness of acupuncture for treating phantom limb syndrome.

Why have I been invited?
You have been chosen to participate in this study if you are:

- 18 years of age or above
- Able to communicate in English (written and verbal)
- An inpatient at the Amputee Rehabilitation Unit
- A lower limb amputee
- Currently suffering from phantom limb syndrome. (This is pain / sensations in your missing limb. It is not pain which is only in your stump. It may however present as pain / sensation in both your stump AND your missing limb).

Do I have to take part?
It is up to you to decide whether or not to take part. We will describe the study and go through the information sheet with you. If you agree to take part, we will then ask you to sign a consent form. You are still free to withdraw at any time, without giving a reason. A decision to withdraw or decision not to take part will not affect the standard of care you receive.

What will happen to me if I take part?
If you are willing to participate, you will randomly be allocated to either receive a course of acupuncture (alongside your usual care) or continue receiving usual care.

Acupuncture Group
If you are allocated to receive acupuncture you will be invited to receive 8 sessions of acupuncture twice weekly over a 4 week period at the Amputee Rehabilitation Unit whilst you are an inpatient here (in addition to your usual programme of care).

Each acupuncture treatment will take about 1 hour and will be arranged on an agreeable day and at a time to suit you. At your initial appointment the practitioner treating you will ask you detailed questions to gain a thorough understanding of your phantom limb syndrome. This will include asking questions about your current symptoms as well as such things as your sleeping pattern, appetite, digestion and emotional wellbeing. Women may also be asked about their menstrual cycle and past pregnancies and childbirths. The practitioner may also take your pulse, examine your tongue and feel for areas of muscular tension or pain. Based on all the information you have given, the practitioner will make a diagnosis and put together your treatment plan.
Acupuncture will involve using very fine single-use, pre sterilised needles to stimulate specific points on your body. Because energy meridians range across the whole body, the points used may not necessarily be close to where you experience your pain or discomfort. Electro-acupuncture may be used as part of treatment. During the time you have acupuncture you will still receive all other usual care provided at the Amputee Rehabilitation Unit.

Alongside receiving acupuncture you will also be asked to complete some assessment questionnaires to evaluate the effectiveness of this treatment. These questionnaires will be completed before you start your acupuncture treatment and then weekly whilst you are receiving acupuncture. It is expected the questionnaires should take no longer than 20 minutes to complete and you will complete them five times in total. You will also be asked to use a sterile swab to collect some cells from the inside of your mouth for genetic analysis of the cortisol receptor. This will take no more than two minutes, does not hurt and does not have to be repeated. You are being asked to do this to see if you can use the swabs correctly. The swabs may help determine people who are likely to respond well to acupuncture. This will be stored anonymously at Kings College and destroyed and disposed of at the end of the study.

<u>Usual Care</u>
If you are allocated to receive usual care, you will continue this, but will also be asked to complete some assessment questionnaires to help us evaluate the effectiveness of acupuncture intervention. These questionnaires will be completed once a week over a five week period of time. The questionnaires should take no longer than 20 minutes to complete and you will complete them five times in total. You will also be asked to use a sterile swab to collect some cells from the inside of your mouth for genetic analysis of the cortisol receptor. This will take no more than two minutes, does not hurt and does not have to be repeated. You are being asked to do this to see if you can use the swabs correctly. The swabs may help determine people who are likely to respond well to acupuncture. This will be stored anonymously at Kings College and destroyed and disposed of at the end of the study.

<u>At the end of your participation in the study</u>
At the end of your participation in the study you may be invited to attend an interview with the researcher. If you are still an inpatient at the Amputee Rehabilitation Unit the interview will take place here. If you have been discharged from the unit the interview will take place either at your home or at the Amputee Rehabilitation Centre depending on which you prefer. The interview will last approximately 1 hour and will be arranged at an agreeable date and time to suit

you. During the interview, the researcher will ask you questions about your experience of being involved in the study, your opinion on the effectiveness of the course of acupuncture, your experience in completing the assessment questionnaires and any negative effects or experiences from being involved in the study. For accuracy of information the interview will be audio recorded as well as notes taken during the interview.
You will only be asked to give one interview. Any published work from the interviews may contain direct quotes from your interview but these will be recorded under a pseudo name / numerical code.

One and three months after the end of your involvement in the study you will be posted and asked to complete the same assessment questionnaires as you completed whilst you were part of the study. As before these should take no more than 20 minutes of your time.
The overall study is planned to last approximately 9 months

Expenses and payments
This study is being undertaken with no funding so no expenses will be given for your time.

What will I have to do?
You may be invited to complete a course of acupuncture alongside your usual care or you may continue receiving usual care. Everyone will be required to have a swab taken once only and also complete assessment questionnaires once weekly for five weeks and at one month and three months post this. 5 participants will be invited to attend a one off interview with the researcher after completion of participation in the study. If you are not invited to complete a course of acupuncture, but you wish to receive it, at the end of your participation in the study you may be referred for acupuncture.

What are the possible disadvantages and risks of taking part?
It is not anticipated that there are any serious risks associated with this study. However, acupuncture may cause some bleeding and / or bruising around the point and sometimes pain after needling a point. Some people report feeling tired and drowsy after treatment and occasionally people feel nausea and / or faint (but this can usually be avoided by treating you lying down and ensuring you are not hungry when you have treatment). Acupuncture may cause a flare up of your symptoms. However, research has shown that acupuncture is relatively safe compared with other forms of treatment.

What are the possible benefits of taking part?
Acupuncture has been shown to be effective in treating other pain conditions and a course of acupuncture may help your phantom limb syndrome. Additionally, many people find acupuncture relaxing and calming and you may benefit from these side effects.
The information you share with the researcher will help with the development of acupuncture protocols for the treatment of phantom limb syndrome.

What if there is a problem?

Any adverse effects which you believe may be associated with acupuncture should be reported. You can do this by telling your practitioner at your next acupuncture appointment. You may also report any adverse effects to a member of staff at the Amputee Rehabilitation Unit. Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

This completes part 1.
If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

Part 2

What will happen if I don't want to carry on with the study?
You are free to withdraw from the study and not have your information included, at any time up to the time of completion of this study. However, after that time, it would be impossible for us to comply.

What if there is a problem?

If you have a concern about any aspect of this study, you should ask to speak with the researcher who will do their best to answer your questions (Esmé Trevelyan: tel: 020 7815 8349 email: trevelye@lsbu.ac.uk). If you wish any further information regarding this study or have any complaints about the way you have been dealt with during the study or other concerns you can contact the director of studies: Prof Nicola Robinson at London South Bank university; tel: 0207 815 7940, who is the Academic Supervisor for this study. Finally, if you remain unhappy and wish to complain formally, you can contact PALS. Tel: 020 7188 8801 or 020 7188 8803. Email: pals@gstt.nhs.uk or the Chair of the University Research Ethics Committee (email ethics@lsbu.ac.uk). Details can be obtained from the university website: https://my.lsbu.ac.uk/page/research-degrees-ethics.

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal action for compensation against London South Bank University who are the sponsors of the study but you may have to pay your legal costs.

Will my taking part in this study be kept confidential?
This study is being completed as part of a MPhil / PhD degree at London South Bank University. It has been reviewed and ethically approved by the London

South Bank University Research Ethics Committee and the National Health Service Research Ethics Committee. All information received from you will be handled in a confidential manner. If you join the study, some parts of the data collected for the study will be looked at by authorised persons from London South Bank University. They may also be looked at by authorised people to check that the study is being carried out correctly. All will have a duty under the Data Protection Act of confidentiality to you as a research participant and we will do our best to meet this duty. All information will be stored in a locked filing cabinet and on a password protected computer in an environment locked when not occupied. Any reference to you will be coded. This information will be held for 5 years before being disposed of securely. Data will not be retained for the use in future studies. Your GP will be informed of your participation in the study only if you consent for us to do so.

What will happen to the results of the research study?
Results of the study will be made available to you if you so wish and you will be invited to give any feedback to us about the results of the study. If you do wish to receive the results of the study we will send them to you when they become available.
The research may be published. Any published work will use a numerical code to protect your identity.

Who is organising and funding the research?
The research is organised by London South Bank University and funded by Guy's and St Thomas' Charity. It is an educational project and is being carried out under the supervision of Prof Nicola Robinson at London South Bank University.

Who has reviewed the study?
All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion London - Bloomsbury Research Ethics Committee.

Further information and contact details
If you need further general information about research, specific information about this project or advice on participation please contact Esmé Trevelyan (tel: 0207815 8349. Email: trevelye@lsbu.ac.uk) or contact a member of the clinical team at the Amputee Rehabilitation Unit (Jodie Georgiou / physiotherapist).

Appendix 6.3 Participant consent form for feasibility study

London South Bank University

A CATALYST FOR INNOVATION IN HEALTH

GUY'S & ST THOMAS' CHARITY

Guy's and St Thomas' NHS
NHS Foundation Trust

Esme Trevelyan
Faculty of Health and Social Care
London South Bank University
103 Borough Road
SE1 0AA
Tel: 0207815 8349
Email: trevelye@lsbu.ac.uk

Amputee Rehabilitation Unit
Lambeth Community Care Centre
Monkton Street
London
SE11 4TX

Tel: 0203 0496912

Ethics Number: 14/LO/0817
Version Number: 02 Date: 11.06.2014
Name of researcher: Esme Trevelyan
Patient Identification Number for this trial:…….

CONSENT FORM
Acupuncture for the treatment of Phantom Limb Syndrome 2

	Please initial to confirm
I confirm that I have read and understand the information sheet dated 11.06.2014 (version 02) for the above study.	•
I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.	•
I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.	•
I understand that relevant sections of any of my medical notes and data collected during the study, may be looked at by responsible individuals from London South Bank University, from regulatory authorities or from Guy's and St Thomas' NHS Foundation Trust. I give permission for these individuals to have access to my records.	•
I consent to my cheek cells being collected to analyse the DNA sequence for the receptor for the hormone cortisol.	
If interviewed I consent to the use of audio-taping during the interview with possible use of verbatim quotations in the research project	
I consent to my GP being informed (by letter) about my participation in this study	
I agree to take part in the above research study.	•

(Name of Participant)	(Signature)	(Date)

(Name of Researcher)	(Signature)	(Date)

When complete, 1 copy for patient: 1 copy for researcher site file: 1 to be kept in medical notes.

Appendix 6.4 Data collection forms for feasibility study

London South Bank University

A CATALYST FOR INNOVATION IN HEALTH

GUY'S & ST THOMAS' CHARITY

Guy's and St Thomas' NHS

NHS Foundation Trust

Ethics Number: 14/LO/0817

Version Number: 01 Date: 2.05.2014

Name of researcher: Esme Trevelyan

Acupuncture for the treatment of Phantom Limb Syndrome 2

Patient Identification Number for this trial:…….

Demographic and Clinical Information

Date:……..

Patient ID:……

DOB:	……..	
Gender:	M [ ] F [ ]	
Ethnicity number (1-18):	.....	
Marital Status	Single [ ] Married / Partner [ ]	Divorced [ ] Widowed [ ]
Education level:	No school qualifications [ ] O level / GCSE [ ]	A Level [ ] University degree [ ]
Occupation:	……...	
Employment status:	Working [ ] Sick leave [ ]	Retired [ ] Unemployed [ ]

Amputation History

Date of amputation:	……..	
Limb amputated:	Right [ ] Left [ ]	Bilateral [ ]
Level of amputation:	Below knee [ ] Through knee [ ]	Above knee [ ] Hip disarticulation [ ]
Reason for amputation:	Vascular [ ] Disease / Tumour [ ] Infection [ ]	Trauma [ ] Other [ ]
Past amputations:	Yes [ ] No [ ]	If yes date of past amputation.....

General Health

Allergies to metal	Yes [ ] No [ ]	
Diabetes	Type I [ ] Type II [ ]	No [ ]
Haemophilia or other bleeding / clotting disorder	Yes [ ] No [ ]	
Anti-coagulant medication	Yes [ ] No [ ]	
Pacemaker	Yes [ ] No [ ]	
Fits / epilepsy	Yes [ ] No [ ] If yes are they controlled:	Yes [ ] No [ ]
Immuno-compromised (e.g. HIV +ve / recently undergone chemotherapy)	Yes [ ] No [ ]	
Lymph nodes removed	Yes [ ] No [ ]	If yes limb affected:……
Pregnant	Yes [ ] No [ ] N/A [ ]	
Wound Health	Good / wound healed [ ]	Poor / wound not healed [ ]

Medical and Drug History:

List of other health problems:

…….....

……..

List of current medications:

……..……..……

……..……

Pain History

Pain in amputed limb prior to amputation	Yes [ ] No [ ]
If yes is phantom pain the same as the pain prior to amputation	Yes [ ] No [ ]

Current / Recent Treatments:

	Prior to admission to ARU	***Whilst at ARU***
Stump massage	Yes [ ] No [ ]	Yes [ ] No [ ]
Desensitising exercises eg touching / stroking stump	Yes [ ] No [ ]	Yes [ ] No [ ]
Graded motor imagery eg left / right limb discrimination, use of mirror box	Yes [ ] No [ ]	Yes [ ] No [ ]
General exercise / stretching / rehabilitation	Yes [ ] No [ ]	Yes [ ] No [ ]
Early walking aid	Yes [ ] No [ ]	Yes [ ] No [ ]
Prosethic use	Yes [ ] No [ ]	Yes [ ] No [ ]
Compression sock	Yes [ ] No [ ]	Yes [ ] No [ ]
Counselling	Yes [ ] No [ ]	Yes [ ] No [ ]

Current Mobility Levels:

Prosthesis	Yes [ ] No [ ]	
Current mobility:	Wheel chair [ ] Walking with assistance [ ]	Walking independenlty [ ]

What is your ethnic group?

Choose one option that best describes your ethnic group or background

White

1. English / Welsh / Scottish / Northern Irish / British
2. Irish
3. Gypsy or Irish Traveller
4. Any other White background, please describe

Mixed / Multiple ethnic groups

5. White and Black Caribbean
6. White and Black African
7. White and Asian
8. Any other Mixed / Multiple ethnic background, please describe

Asian / Asian British

9. Indian
10. Pakistani
11. Bangladeshi
12. Chinese
13. Any other Asian background, please describe

Black / African / Caribbean / Black British

14. African
15. Caribbean
16. Any other Black / African / Caribbean background, please describe

Other ethnic group

17. Arab
18. Any other ethnic group, please describe

recommended country specific ethnic group question for use in England. This question is recommended when a show card is used in a face-to-face interview or self-completion survey (both paper and electronic).

Office for National Statistics

http://www.ons.gov.uk/ons/guide-method/measuring-equality/equality/ethnic-nat-identity-religion/ethnic-group/index.html

Numerical Pain Rating Scale

This is a rating scale (11 point scale i.e. 0 to 10) of pain where 0 = no pain and 10 = pain as bad as you can imagine.

1. Please rate your phantom pain (pain in your missing leg) by choosing the one number that best describes your pain on average over the last week:

0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10

No Pain **Pain as bad as you can imagine**

2. Please rate your phantom pain (pain in your missing leg) by choosing the one number that best describes the worst pain you have experienced over the last week

0 - 1 - 2 - 3 - 4 - 5 - 6 - 7 - 8 - 9 - 10

No Pain **Pain as bad as you can imagine**

Short-Form McGill Pain Questionnaire-2 (SF-MPQ-2)

This questionnaire provides you with a list of words that describe some of the different qualities of pain and related symptoms. Please put an **X** through the numbers that best describe the intensity of each of the pain and related symptoms you felt during the past week. Use 0 if the word does not describe your pain or related symptoms.

1. Throbbing pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
2. Shooting pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
3. Stabbing pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
4. Sharp pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
5. Cramping pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
6. Gnawing pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
7. Hot-burning pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
8. Aching pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
9. Heavy pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
10 Tender	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
11 Splitting pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
12 Tiring-exhausting	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
13 Sickening	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
14 Fearful	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
15 Punishing-cruel	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
16 Electric-shock pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
17 Cold-freezing pain	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
18 Piercing	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
19 Pain caused by light touch	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
20 Itching	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
21 Tingling or 'pins and needles'	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
22 Numbness	*none*	**0**	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**

Insomnia Severity Index

For each question, please *CIRCLE* the number that best describes your answer.

Please rate the *CURRENT (i.e. LAST 2 WEEKS) SEVERITY* of your insomnia problem(s).

Insomnia problem	None	Mild	Moderate	Severe	Very severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problem waking up too early	0	1	2	3	4

4. How SATISFIED/DISSATISFIED are you with your CURRENT sleep pattern?

Very Satisfied	Satisfied	Moderately Satisfied	Dissatisfied	Very Dissatisfied
0	1	2	3	4

5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life?

Not at all Noticeable	A Little	Somewhat	Much	Very Much Noticeable
0	1	2	3	4

6. How WORRIED/DISTRESSED are you about your current sleep problem?

Not at all Worried	A Little	Somewhat	Much	Very Much Worried
0	1	2	3	4

7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) CURRENTLY?

Not at all Interfering	A Little	Somewhat	Much	Very Much Interfering
0	1	2	3	4

Used with permission from Charles M. Morin, Ph.D., Université Laval

PSS-10

INSTRUCTIONS:

The questions in this scale ask you about your feelings and thoughts during the last month. In each case, please indicate your response by placing an "X" over the circle representing HOW OFTEN you felt or thought a certain way.

	Never 0	Almost Never 1	Sometimes 2	Fairly Often 3	Very Often 4
1. In the last month, how often have you been upset because of something that happened unexpectedly?	O	O	O	O	O
2. In the last month, how often have you felt that you were unable to control the important things in your life?	O	O	O	O	O
3. In the last month, how often have you felt nervous and "stressed"?	O	O	O	O	O
4. In the last month, how often have you felt confident about your ability to handle your personal problems?	O	O	O	O	O
5. In the last month, how often have you felt that things were going your way?	O	O	O	O	O
6. In the last month, how often have you found that you could not cope with all the things that you had to do?	O	O	O	O	O
7. In the last month, how often have you been able to control irritations in your life?	O	O	O	O	O
8. In the last month, how often have you felt that you were on top of things?	O	O	O	O	O
9. In the last month, how often have you been angered because of things that were outside your control?	O	O	O	O	O
10. In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	O	O	O	O	O

Hospital Anxiety and Depression Scale (HADS)

GL assessment
the measure of potential

Name: _____ Date: _____

FOLD HERE

Clinicians are aware that emotions play an important part in most illnesses. If your clinician knows about these feelings he or she will be able to help you more.

This questionnaire is designed to help your clinician to know how you feel. Read each item below and **underline the reply** which comes closest to how you have been feeling in the past week. Ignore the numbers printed at the edge of the questionnaire.

Don't take too long over your replies, your immediate reaction to each item will probably be more accurate than a long, thought-out response.

A	D			A	D
		I feel tense or 'wound up'	**I feel as if I am slowed down**		
3		Most of the time	Nearly all the time		3
2		A lot of the time	Very often		2
1		From time to time, occasionally	Sometimes		1
0		Not at all	Not at all		0
		I still enjoy the things I used to enjoy	**I get a sort of frightened feeling like 'butterflies' in the stomach**		
	0	Definitely as much	Not at all	0	
	1	Not quite so much	Occasionally	1	
	2	Only a little	Quite often	2	
	3	Hardly at all	Very often	3	
		I get a sort of frightened feeling as if something awful is about to happen	**I have lost interest in my appearance**		
3		Very definitely and quite badly	Definitely		3
2		Yes, but not too badly	I don't take as much care as I should		2
1		A little, but it doesn't worry me	I may not take quite as much care		1
0		Not at all	I take just as much care as ever		0
		I can laugh and see the funny side of things	**I feel restless as if I have to be on the move**		
	0	As much as I always could	Very much indeed	3	
	1	Not quite so much now	Quite a lot	2	
	2	Definitely not so much now	Not very much	1	
	3	Not at all	Not at all	0	
		Worrying thoughts go through my mind	**I look forward with enjoyment to things**		
3		A great deal of the time	As much as I ever did		0
2		A lot of the time	Rather less than I used to		1
1		Not too often	Definitely less than I used to		2
0		Very little	Hardly at all		3
		I feel cheerful	**I get sudden feelings of panic**		
	3	Never	Very often indeed	3	
	2	Not often	Quite often	2	
	1	Sometimes	Not very often	1	
	0	Most of the time	Not at all	0	
		I can sit at ease and feel relaxed	**I can enjoy a good book or radio or television programme**		
0		Definitely	Often		0
1		Usually	Sometimes		1
2		Not often	Not often		2
3		Not at all	Very seldom		3

Now check that you have answered all the questions

	A	D
TOTAL		

PGIC

Chief Complaint (Presenting Problem):_____

Since being enrolled in this study, how would you describe the change (if any) in ACTIVITY LIMITATIONS, SYMPTOMS, EMOTIONS, and OVERALL QUALITY OF LIFE in relation to your phantom limb pain?

Please circle the number below, that matches your degree of change since beginning care at this clinic for the above stated chief complaint.

No change	Almost the same	A little better	Somewhat better	Moderately better	Better	A great deal better
1	2	3	4	5	6	7

Explanation:

1 = No change (or condition has got worse)
2 = Almost the same, hardly any change at all
3 = A little better, but no noticeable change
4 = Somewhat better, but the change has not made any real difference
5 = Moderately better, and a slight but noticeable change
6 = Better, and a definite improvement that has made a real and worthwhile difference
7 = A great deal better, and a considerable improvement that has made all the difference

Under each heading, please tick the ONE box that best describes your health TODAY

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

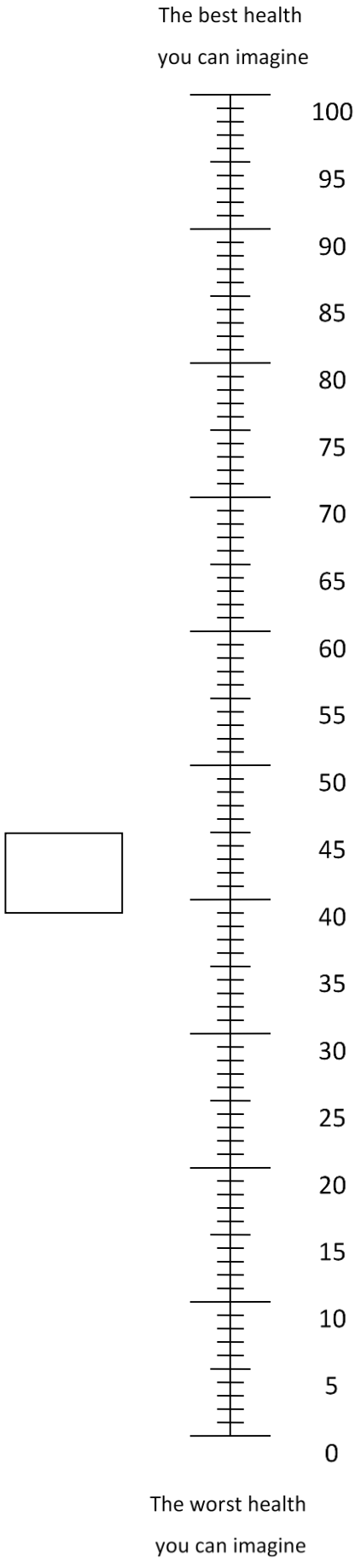
I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

- We would like to know how good or bad your health is

TODAY.

- This scale is numbered from 0 to 100.
- 100 means the <u>best</u> health you can imagine.
  0 means the <u>worst</u> health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY =



Appendix 6.5 Hospital anxiety and depression scale licence

(b) If the Licensee shall at any time be in breach of any of the terms and conditions of this Agreement and if capable of being remedied, such breach is not remedied within 15 days of receipt of written notice thereof; or

(c) If the Licensee is declared insolvent or bankrupt or goes into liquidation (other than voluntary liquidation for the purpose of reconstruction only) or if a Receiver is appointed or if the Licensee is subject to any similar event anywhere in the world.

Termination shall be without prejudice to any monies which may be due to the Publishers from the Licensee and without prejudice to any claim which the Publishers may have for damages and/or otherwise.

Upon termination of this Agreement for any reason the Licensee shall immediately cease to use the Material.

15. This Agreement constitutes the entire agreement between the parties in respect of the Material and supersedes all prior oral or written proposals, agreements or undertakings concerning the same.

16. This Agreement shall not be amended or modified in any way other than by an agreement in writing and signed by both parties or their duly authorised representatives and shall come into effect on receipt of the payment in full as specified above and a counter-signed copy of this Agreement.

17. This Agreement shall be governed by and construed in all respects in accordance with English Law and the courts of England and Wales shall have exclusive jurisdiction to settle any dispute arising out of or in connection with this Agreement, its subject matter and formation, including non-contractual disputes or claims.

AS WITNESS THE HANDS OF THE PARTIES
hereto the day and year first above written

Signed on behalf of GL Assessment Limited

S Green 29/07/14

Signed by the Licensee: ***Please print this page, sign, and attach this signature page as a scanned document along with your typed User Agreement form, sent as a Word doc***

User's Signature (handwritten):	**Company/Organisation Stamp (if applicable):**
Title: MRS	Faculty of Health and Social Care London South Bank University 103 Borough Road London SE1 0AA
Company/Organisation: LONDON SOUTH BANK UNIVERSITY	
Date: 17/7/2014	

ACCOUNT NO:- 102890

Appendix 6.6 Interview topic guide for feasibility study

Interview Topic Guide

Acupuncture for the treatment of phantom limb syndrome 2

Date of interview:……..

Study ID number:……

Objectives

- To explore the feasibility of randomising and retaining participants in the study
- To evaluate the acceptability of acupuncture as an intervention
- To explore the perceived effectiveness of acupuncture in treating phantom limb syndrome and other secondary symptoms
- To identify appropriate primary and secondary outcome measures which could be used in future trials
- To explore participants experience in completing outcome measures and taking part in the research study

Introduction

Explain the items that will be covered in the interview, confidentiality and length of time of interview

(I would like to talk with you about your experience of being in the study and having acupuncture. I also would like to talk about how effective you found acupuncture at treating PLP and your experience of completing the questionnaires).

Introduction

Could you tell me about any past experience you have had of acupuncture before being in this study.

1. Reasons – *why did you have acupuncture?*
2. Number of treatments – *how many treatments did you have?*
3. What did treatments involve (moxa / cupping/ EA / auricular) – *can you tell me about a typical acupuncture treatment?*
4. Did you enjoy treatments – *did you like having acupuncture or not / why?*
5. Did treatments help – *can you tell me about any positive or negative effects you experienced from acupuncture?*

Study specific questions

What were your initial thoughts when you were told about the study?

What made you decide to participate in the study?

How did you feel when you found out that you were going to have acupuncture?

What were your expectations of having acupuncture / what did you expect to get out of having acupuncture?

Did you think acupuncture could help treat your PLP?

Acupuncture Treatment

Can you tell me about your experience of having acupuncture?

1. *Can you describe one of your treatments to me?*
2. *Can you tell me what your practitioner told you about the treatment?*
3. *Where did you have the acupuncture needles / was there anywhere you didn't like having needles / why?*
4. *Did you have EA / what did you think of the EA?*
5. *What was it like having treatment?*
6. *How did you feel when you were having treatment?*
7. *What was your PLP like whilst you were having treatment?*
8. *Did you like or dislike having treatment / why?*

Overall, do you think the acupuncture has had any effect on your PLP (good or bad)?

1. *How many treatments did you have before you started noticing an effect on you PLP?*
2. *How did your PLP change (intensity / frequency or quality)?*
3. *How do you feel about your PLP compared to when you started treatment?*
4. *Do you think the acupuncture made you see your PLP differently / if so how?*
5. *Do you think the acupuncture treatment worked for your PLP?*

Can you tell me about any other physical effects you noticed from having had the course of acupuncture?

1. *Has it had any effect on any other pains you had / any change in activity levels because of the acupuncture?*

Can you tell me about any effects the acupuncture had on your general wellbeing?

1. *Some people say acupuncture can make you have more energy / feel tired / relaxed / changes in sleep patterns. Did you notice any of these kinds of effects?*

Can you tell me about any bad effects you have experienced from the acupuncture?

1. *Some people say acupuncture is painful (pain from the needles) / can aggravate pain / can make you feel faint / tired?*

Could you tell me about your relationship with your practitioner?

In terms of frequency of treatments, do you feel twice a week was about right for treating your phantom limb pain or do you feel you needed more / less frequent treatments (why)?

In terms of number of treatments, do you feel 8 was too few / too many (why)?

Did the course of acupuncture disrupt your routine here at the ARU and if so how?

1. *How did your find having 2 treatments a week (too much / too few)?*
2. *Was there anything that made it hard for you to have two treatments a week?*

Experience of treatment

Did the course of acupuncture live up to your expectations?

1. *Overall what did you particularly like or dislike about the acupuncture treatments?*
2. *Did you get what you were hoping for out of the acupuncture treatments?*
3. *Are you happy with the treatment you received?*
4. *Is there anything you didn't like about the treatments?*
5. *Is there anything you think we should change about the treatments?*

Would you recommend acupuncture to other people with PLP?

If it was offered would you like to continue your course of acupuncture now?

1. *Why would you like / not like to continue your course of acupuncture now?*

In the future would you consider using acupuncture to treat other health problems you may have?

Completing questionnaires (outcome measures)

How did you find completing the questionnaires?

1. *Do you think you benefitted at all from filling in the questionnaires (how)?*
2. *Do you think filling in the questionnaires had and negative effects on you?*

Was the length of time it took to complete the questionnaires acceptable to you or did it take too long?

Did you find the questionnaires easy to complete?

Did you think the questionnaires fully captured your experience of phantom limb pain?

1. *Do you think we should ask anything else about PLP?*

If you could only fill in one questionnaire which one would you choose and why?

Which questionnaires did you like the least and why?

Do you think it was relevant and appropriate to ask about your sleep and mood as well

as asking about your PLP?

Was there anything you think we should have asked about which we didn't?

Summary

Overall did you have any problems / bad experiences during your participation in this study?

If we did this study again is there anything you would advise we change?

Is there anything else you would like to mention about your experience of being involved in this study?

In a sentence could you sum up your experience of being involved in this study?

Appendix 6.7 Ethical approval letter from NRES Committee London – Bloomsbury, and London South Bank University for feasibility study

London South Bank University

Direct line: 020-7815 6025
E mail: mitchen5@lsbu.ac.uk
Ref: UREC 1458

Esme Trevelyan
Faculty of Health and Social Care
London South Bank University
103 Borough Road
SE1 0AA

Thursday 16 October 2014

Dear Esme

RE: Acupuncture for the treatment of phantom limb syndrome (2)

Thank you for submitting this proposal and for your response to the reviewers' comments.
I am pleased to inform you that Full Chair's Approval has been given by Chair on behalf of the University Research Ethics Committee.

I wish you every success with your research. Yours sincerely,

Nicola Mitchell

Secretary, LSBU Research Ethics Committee

cc:

Prof Shushma Patel, Chair, LSBU Research Ethics Committee

NHS
Health Research Authority

National Research Ethics Service

NRES Committee London – Bloomsbury

HRA NRES Cente Manchester
Barlow House 3rd Floor
4 Minshull Street
Manchester
M1 3DZ
Telephone: 0161 625 7815
Fax: 0161 625 7299

12 November 2014

Professor Nicola Robinson
Professor of Traditional Chinese Medicine (TCM) and Integrated Health
London South Bank University
Faculty of Health and Social Care
London South Bank University
103 Borough Road
SE1 0AA

Dear Professor Robinson

Study title: **Acupuncture for the treatment of Phantom Limb Syndrome: A randomised feasibility study**
REC reference: **14/LO/0817**
IRAS project ID: **152726**

Thank you for your email of 14 October 2014. I can confirm the REC has received the documents listed below and that these comply with the approval conditions detailed in our letter dated 29 July 2014.

Documents received

The documents received were as follows:

Document	*Version*	*Date*
Other [Confirmation of R&D approval]		14 October 2014

Approved documents

The final list of approved documentation for the study is therefore as follows:

Document	*Version*	*Date*
Covering letter on headed paper		12 June 2014
Covering letter on headed paper		02 May 2014
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)	Zurich Municipal	18 July 2013
GP/consultant information sheets or letters	2	11 June 2014
Interview schedules or topic guides for participants	01	02 May 2014

Letter from sponsor	LSBU	31 March 2014
Letter from statistician	Nichola Crichton	07 July 2014
Non-validated questionnaire [McGill SF-MPQ-2]	Validated	
Non-validated questionnaire [Health Questionnaire EQ-5D-5L]	Validated	
Non-validated questionnaire [Demographic and Clinical Information]	01	02 May 2014
Other [Confirmation of R&D approval]		14 October 2014
Other [The effectiveness of acupuncture/TENS for phantom limb syndrome II]		
Other [Letter from Funder - Guys & St. Thomas' Charity]		29 April 2014
Other [email regarding statistical review]		01 July 2014
Other [The effectiveness of acupuncture/TENS for phantom limb syndrome I]		
Participant consent form	2	11 June 2014
Participant information sheet (PIS)	2	11 June 2014
REC Application Form	3.5	01 May 2014
Referee's report or other scientific critique report [The effectiveness of acupuncture/TENS for phantom limb syndrome II]	European Journal of Integrative	
Referee's report or other scientific critique report [The effectiveness of acupuncture/TENS for phantom limb syndrome I]	European Journal of Integrative	
Research protocol or project proposal	01	02 May 2014
Response to Request for Further Information		02 July 2014
Summary CV for Chief Investigator (CI)	Nicola Robinson	01 May 2014
Summary CV	Esme Trevelyan	02 May 2014
Summary CV	Warren Turner	06 August 2013
Validated questionnaire [PGIC Scale]	Validated	
Validated questionnaire [PSS]	Validated	
Validated questionnaire [Hospital Anxiety & Depression Scale]	Validated	
Validated questionnaire [Numerical Pain Rating Scale]	01	02 May 2014
Validated questionnaire [Insomnia Severity Index]	Validated	

You should ensure that the sponsor has a copy of the final documentation for the study. It is the sponsor's responsibility to ensure that the documentation is made available to R&D offices at all participating sites.

14/LO/0817 **Please quote this number on all correspondence**

Yours sincerely

Dr Ashley Totenhofer
REC Manager
E-mail: nrescommittee.london-bloomsbury@nhs.net

Copy to: Professor Nicola Crichton – London South Bank University

Ms Karen Ignatian - Guy's And St Thomas' NHS Foundation Trust

Appendix 6.8 Acupuncture points used by practitioners during the feasibility study

Residual limb	F	Contralateral limb	F	Body points	F	Points on Lx	F	Auricular acupuncture	Upper limb points to treat lower limb	F
Sp 8	2	Sp 3	1	Yintang	1	Bl 23	5	Yes X 2*	LI 2	1
Sp 9	9	Sp 4	9	Du 20	1	Bl 24	3		LI 4	4
Sp 10	20	Sp 5	18	LI4	1	Bl 25	5		LI 5	2
Sp 11	1	Sp 6	17			Bl 26	5		LI 6	1
		Sp 9	17			Bl 27	2		LI 10	3
St 32	1	Sp 10	11			Bl 50	1		LI 11	4
St 33	1					Bl 52	1			
St 34	16	St 34	2						Lu 9	1
St 35	16	St 35	7			Du 4	3			
St 36	8	St 36	8						PC6	1
St 37	1	St 41	11			GB 29	2		PC7	1
		St 42	2			GB 30	2			
GB 34	4	St44	5						TB 5	1
GB 35	1					Huatuojiaji	1			
		GB 34	5							
LR 8	4	GB 39	5							
		GB 40	6							
Heding	2	GB 42	1							
Xiyan	14	GB 43	1							
Ashi point	1									
		LR2	4							
		LR3	8							
		LR8	4							
		Bl 57	1							
		Bl 58	4							
		Kid 3	7							
		Kid 5	3							
		Kid 6	2							
		Kid 7	2							
		Kid 10	1							
		Xiyan	4							
		Ashi Points	2							
		Heding	2							
		Bafeng	1							
Other: Cupping Tx, F X 1 Points for the shoulder, F X 9										

Key: F, frequency; *, acupuncture points not recorded; Tx, thoracic area; Sh, shoulder; pts, acupuncture points.
**Points for the shoulder: LI 14, LI 15, LI 16, TB 13, TB 14 SI 14, SI 15, Jianqian, ashi points.